

*Saunders Handbook of*  
**VETERINARY  
DRUGS**

Small and Large Animal

FOURTH EDITION

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SAUNDERS HANDBOOK OF VETERINARY DRUGS: SMALL  
AND LARGE ANIMAL, FOURTH EDITION

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*This is dedicated to the veterinary students whom  
I've had the pleasure to teach over the years. I have learned more  
from them than they realize, and their input and inspiration have  
stimulated much of the work in this fourth edition. As they enter the  
challenging veterinary profession, it is my hope that this book will  
facilitate safe and effective use of medicines in their patients and  
encourage them to keep reading and never stop learning.*

**Mark G. Papich**

## DISCLAIMER

Doses listed are species specific, unless otherwise listed. There is no assurance for safety and efficacy in other animal species not listed. Many of the doses listed are extralabel or are human drugs used in an off-label or extralabel manner. Federal regulations allow use of extralabel veterinary drugs and human drugs in non-food-producing animals when there is a valid veterinarian–client–patient relationship. However, there are restrictions for using these drugs in food-producing animals under the Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1994. Requirements under this act can be found at the website of the American Veterinary Medical Association (AVMA): <https://www.avma.org/KB/Resources/Reference/Pages/AMDUCA.aspx>. Extralabel use of drugs is prohibited from use in food-producing animals unless certain requirements are met, which include extended withdrawal times for meat and milk.

Doses listed are based on best available evidence at the time of the drug handbook preparation; however, the author cannot ensure efficacy of drugs used according to recommendations in this book. Other patient factors or actions of the drug not known at the time of the book preparation may affect efficacy. Adverse effects of which the author was not aware at the time of the handbook's preparation may be possible from drugs listed in this handbook.

Veterinarians using this handbook are encouraged to check current literature, product label, federal Freedom of Information (FOI), and the manufacturer's disclosure for information regarding efficacy and any known adverse effects or contraindications not identified at the time of preparation of this handbook.

**Mark G. Papich**

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## Preface

The fourth edition of this handbook was developed using a similar style, layout, and format as the previous edition to ease the transition for users of earlier versions. Additions, changes in individual drug monographs, and expanded sections were provided with input and helpful suggestions from veterinarians, drug sponsors, and students or because new information has become available in the published literature. New drugs that have been approved by the U.S. Food and Drug Administration (FDA), or for which there is new information about its use in the literature, have been added. The drugs listed represent the most important medications used in companion animals and livestock. Practically every drug monograph has been updated, and more than 20 new drugs have been added. Some discontinued or outdated medications have been deleted, and readers can refer to previous editions of this book for information on those drugs. As in previous editions, this book includes approved drugs for animals in addition to human medications for which veterinary uses have been identified. Information has been updated on clinical uses and regulatory requirements. The information on drug stability, storage, and compounding has been expanded. An increased effort has been made to include evidence-based information on the drug's efficacy and clinical use in the "Indications and Clinical Uses" and "Instructions for Use" sections. To facilitate the location of important information for each medication, the sections are divided into categories for drug interactions, precautions, pharmacology, and clinical use. Tables for quick reference can be found in the appendixes. These appendix tables include antibiotics of choice, drug interactions, regulatory information, phone numbers and Internet sites for drug information, and a section on drug dose calculations.

The book is designed for busy practitioners and students who want to make the most efficient use of their time and locate accurate and reliable drug information quickly. The format is consistent from drug to drug, and veterinarians and their staff will quickly become familiar with the layout of each drug monograph to rapidly locate concise and accurate information about each drug.

In preparing this handbook, my priorities were accuracy and reliability. As in previous editions, the indications for use and drug dosing information were prepared from a review of the literature or input from clinical specialists. In some cases, dosages originated from clinical studies; in other cases, they represent a standard of good clinical practice, even if it is considered extralabel. Manufacturers' recommendations are considered in the dosing recommendations, but other suggestions (extralabel indications and uses) also may be listed where the use and dosage have gone beyond those listed on the product's label. Where dosage recommendations have varied among sources, I have applied my clinical judgment and 30 years of experience in veterinary clinical pharmacology to derive a scientifically valid dose. In some cases, it may have been necessary to derive a dose based on extrapolations from human medicine, but this was limited to drugs for which the therapeutic index of the drug is high. To derive withdrawal times for food animals, the highest priority has been given to the withdrawal time approved by the Food and Drug Administration (FDA). When there was not an FDA-approved withdrawal time, suggestions made by the Food Animal Residue Avoidance Databank (FARAD; [www.farad.org](http://www.farad.org)) were used. If neither of these was available, I listed a conservative estimate for a suggested withdrawal time based on the drug's pharmacokinetics and likelihood that it may cause harmful residues.

Each drug is listed alphabetically by its official name (USAN) that is recognized by the United States Pharmacopeia (USP; [www.usp.org](http://www.usp.org)). Following each drug name is the brand or trade name and synonyms by which the drug also may be known. Innovator brand names are provided, but not all of the brand names available are necessarily listed. The cross-reference table in the front section of the book lists drugs according to their functional classification and drug use. It may not include all of the known uses for a drug, but represents the most common clinical use.

As clinical experience increases and our knowledge of the pharmacology of these drugs expands, new information may become available for the medications listed in this book. I welcome feedback relating to adverse effects observed, clinical experience, and omissions or errors identified. For these and other input and suggestions, I can be reached at [mark\\_papich@ncsu.edu](mailto:mark_papich@ncsu.edu). Adverse drug events also should be reported to the drug sponsor directly or the FDA using this website: [www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/](http://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/).

Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name	Brand Name
Acidifier	Racemethionine	Uroezee, Methio-Form, and generic. Human forms include Pedameth, Uracid, and generic
	Ammonium chloride	Generic
Adrenal suppressant	Trilostane	Modrenal, Vetoryl
Adrenergic agonist	Ephedrine hydrochloride	Many
	Epinephrine	Adrenaline and generic forms
	Fenoldopam mesylate	Corlopam
	Phenylpropanolamine hydrochloride	Brand names of Dexatrim, Propagest, PPA, and others were human over-the-counter (OTC) brands and are now off the market. Veterinary formulations—although not approved by FDA —have been marketed as Proin-ppa, UriCon, and Propalin tablets and syrup.
	Pseudoephedrine hydrochloride	Sudafed
Adrenolytic agent	Mitotane	Lysodren, op-DDD
Alkalinizing agent	Potassium citrate	Generic, Urocit-K
	Sodium bicarbonate	Baking soda, soda mint, citrocarbonate, Arm and Hammer Pure Baking Sod.
Alpha <sub>2</sub> -antagonist	Atipamezole hydrochloride	Antisedan
	Yohimbine	Yobine
Analgesic	Acetaminophen	Tylenol and generic brands
	Amantadine	Symmetrel
	Gabapentin	Neurontin
	Pregabalin	Lyrica
	Tramadol	Ultram and generic
Analgesic, opioid	Hydrocodone bitartrate	Hycodan
	Hydromorphone	Dilaudid, Hydrostat, and generic
	Acetaminophen + codeine	Tylenol with codeine and many generic brands
	Buprenorphine hydrochloride	Buprenex (Vetergesic in the UK)
	Butorphanol tartrate	Torbutrol, Torbugesic
	Fentanyl citrate	Sublimaze
	Fentanyl transdermal	Recuvyra, Duragesic

## Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name	Brand Name
Analgesic, opioid, antitussive	Meperidine	Demerol
	Methadone hydrochloride	Dolophine, Methadose
	Morphine sulfate	Extended-release tablets: MS Contin or Oramorph SR, or generic
	Oxymorphone hydrochloride	Numorphan
	Pentazocine	Talwin-V
	Remifentanyl	Ultiva
	Sufentanyl citrate	Sufenta
	Butorphanol tartrate	Torbutrol, Torbugesic
	Codeine	Codeine phosphate, codeine sulfate
	Hydrocodone bitartrate	Hycodan
Analgesic, nonsteroidal antiinflammatory	Aspirin	ASA, acetylsalicylic acid, Bufferin, Ascriptin, and many generic brands
	Carprofen	Rimadyl (Zinecarp is a European brand name)
	Deracoxib	Deramaxx
	Etodolac	EtoGesic (veterinary); Lodine (human)
	Firocoxib	Previcox
	Flunixin meglumine	Banamine, and generic
	Ibuprofen	Motrin, Advil, Nuprin
	Indomethacin	Indocin
	Ketoprofen	Orudis-KT (human OTC tablet); Ketofen (veterinary injection); Anafen (outside the US)
	Ketorolac tromethamine	Toradol
	Meclofenamate sodium; Meclofenamic acid	Arquel, Meclofen
	Meloxicam	Metacam (veterinary drug), Mobic (human drug), Metacam suspension (equine drug in Europe)
	Naproxen	Naprosyn, Naxen, Aleve (naproxen sodium)
	Phenylbutazone	Butazolidin, PBZ, and generic
	Piroxicam	Feldene and generic
	Robenacoxib	Onsior
	Tepoxalin	Zubrin
	Alfaxalone	Alfaxan
	Ketamine hydrochloride	Ketalar, Ketavet, Vetalar
	Propofol	Rapinivet, Propoflo (veterinary); Diprivan (human)
	Tiletamine and Zolazepam	Telazol, Zoletil

Continued



Listing of Drugs According to Functional and Therapeutic Classification		
Drug Classification	Drug Name	Brand Name
Anesthetic, sedative alpha <sub>2</sub> -agonist	Detomidine hydrochloride	Dormosedan
	Dexmedetomidine	Dexdomitor
	Medetomidine hydrochloride	Domitor
	Romifidine hydrochloride	Sedivet
	Xylazine hydrochloride	Rompun and generic
Anesthetic, barbiturate	Methohexital sodium	Brevital
	Pentobarbital sodium	Nembutal and generic
	Thiopental sodium	Pentothal
Anesthetic, inhalant	Enflurane	Ethrane
	Halothane	Fluothane
	Isoflurane	Aerrane
	Methoxyflurane	Metofane
	Sevoflurane	Aerrane
Antacid	Aluminum hydroxide, and Aluminum carbonate	Aluminum hydroxide gel (Amphogel), aluminum carbonate gel (Basalgel)
Antiarrhythmic	Amiodarone	Cordarone
	Carvedilol	Coreg
	Disopyramide	Norpace (Rythmodan in Canada)
	Lidocaine hydrochloride	Xylocaine
	Mexiletine	Mexitil
	Procainamide hydrochloride	Pronestyl
	Quinidine	Quinidine gluconate: Duraquin
	Quinidine sulfate	Quinidine polygalacturonate: Cardioquin
	Quinidine gluconate	Quinidine sulfate: Cin-Quin, Quinora
	Quinidine polygalacturonate	
Antiarrhythmic, calcium channel blocker	Tocainide hydrochloride	Tonocard
	Diltiazem hydrochloride	Cardizem, Dilacor
	Verapamil hydrochloride	Calan, Isoptin
Antiarthritic agent	Polysulfated glycosaminoglycan	Adequan Canine Adequan IA, Adequan IM
	Chondroitin sulfate	Cosequin, Glycoflex, and other brands
	Glucosamine and chondroitin sulfate	Cosequin, Glycoflex, and other brands
Antibacterial	Chloramphenicol	Chloramphenicol palmitate, Chloromycetin
	Clofazimine	Lamprane

## Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name	Brand Name
Antibacterial, aminoglycoside	Dapsone	Generic
	Florfenicol	Nuflor
	Fosfomycin	Monurol
	Isoniazid	Isonicotinic acid hydrazide
	Linezolid	Zyvox
	Methenamine	Methenamine hippurate: Hiprex, Urex Methenamine mandelate: Mandelamine and generic
	Nitrofurantoin	Macrochantin, Furalan, Furatoin, Furadantin, or generic
	Polymyxin B	Generic
	Pyrimethamine	Daraprim
	Rifampin	Rifadin, Rifampicin
	Amikacin	Amiglyde-V (veterinary), Amikin (human), and generic
	Gentamicin sulfate	Gentocin
	Neomycin	Biosol
	Kanamycin sulfate	Kantrim
	Tobramycin sulfate	Nebcin
Antibacterial, lincosamide	Lincomycin hydrochloride	Lincocin, Lincomix
	Lincomycin hydrochloride monohydrate	
	Clindamycin hydrochloride	Antirobe, Clindrops, Clintabs, Clinsol, and generic (veterinary); Cleocin (human)
	Clindamycin phosphate	
	Clindamycin palmitate	
Antibacterial, macrolide	Azithromycin	Zithromax
	Clarithromycin	Biaxin and generic
	Erythromycin	Many brands and generic; Gallimycin-100, Gallimycin-200, Erythro-100
	Gamithromycin	Zactran
	Tildipirosin	Zuprevo
Antibacterial, potentiated sulfonamide	Tilmicosin phosphate	Micotil, Pulmotil tilmicosin premix
	Tulathromycin	Draxxin, Draxxin 25+C28
	Tylosin	Tylocine, Tylan, Tylosin tartrate
	Ormetoprim and sulfadimethoxine	Primor
	Trimethoprim and sulfadiazine	Tribrissen, Uniprim, Tucoprim, Di-Trim, and others
	Trimethoprim and sulfamethoxazole	Bactrim, Septra, and generic forms

Continued

Listing of Drugs According to Functional and Therapeutic Classification		
Drug Classification	Drug Name	Brand Name
Antibacterial, antidiarrheal	Sulfasalazine	Azulfidine (Salazopyrin in Canada)
	Metronidazole	Flagyl and generic
Antibacterial, antiparasitic	Metronidazole benzoate	
	Metronidazole hydrochloride	
Antibacterial, beta-lactam	Ronidazole	Flagyl and generic
	Amoxicillin	Amoxicillin - Amoxi-Tabs, Amoxi-Drops, Amoxi-Inject, Robamox-V, Biomox, and other brands; Amoxil, Trimox, Wymox, Polymox, (human forms); Amoxicillin trihydrate
	Amoxicillin and clavulanate potassium	Veterinary: Clavamox Human: Augmentin
	Ampicillin	Human forms include Omnipen, Principen, Totacillin, Polycillin. Injectable forms include Omnipen-N, Polycillin-N, Totacillin-N. Veterinary forms include Amp-Equine, and Ampicillin trihydrate (Polyflex).
	Cefaclor	Ceclor
	Cefadroxil	Veterinary: Cefa-Tabs, Cefa-Drops, Human dosage form: Duricef and generic
	Cefazolin sodium	Ancef, Kefzol, and generic
	Cefdinir	Omnicef
	Cefepime	Maxipime
	Cefixime	Suprax
	Cefotetan disodium	Cefotan
	Cefovecin	Convenia
	Cefoxitin sodium	Mefoxin
	Cefpodoxime proxetil	Simplicef (veterinary drug) Vantin (human drug)
	Cefquinome	Cobactan, Cephaguard
	Ceftazidime	Fortaz, Ceptaz, Tazicef, Tazidime.
	Ceftiofur crystalline-free acid	Excede
	Ceftiofur hydrochloride	Excenel
	Ceftiofur sodium	Naxcel
	Cephalexin	Keflex and generic forms
	Cloxacillin sodium	Cloxapen, Orbenin, Tegopen
	Doripenem	Doribax
	Ertapenem	Invanz

**Listing of Drugs According to Functional and Therapeutic Classification**

<b>Drug Classification</b>	<b>Drug Name</b>	<b>Brand Name</b>
Antibacterial, fluoroquinolone	Imipenem and Cilastatin	Primaxin
	Oxacillin sodium	Pro-staphli, and generic
	Penicillin G	Penicillin G potassium or sodium: Many brands Penicillin G benzathine: Benza-Pen, and other names Penicillin G, Procaine: Generic Penicillin V: Pen-Vee
	Piperacillin sodium	Pipracil
	Piperacillin sodium and Tazobactam	Zosyn
	Ticarcillin and clavulanate potassium	Timentin
	Ticarcillin disodium	Ticar, Ticillin
	Ampicillin and sulbactam	Unasyn
	Carbenicillin	Carbenicillin: Geopen, Pyopen Carbenicillin indanyl sodium: Geocillin
	Cefotaxime sodium	Claforan
	Dicloxacillin sodium	Dynapen
	Meropenem	Merrem
	Dicloxacillin sodium	Dynapen
	Meropenem	Merrem
	Ciprofloxacin hydrochloride	Cipro and generic forms
	Danofloxacin mesylate	Advocin
	Difloxacin hydrochloride	Dicural
	Enrofloxacin	Baytril
	Marbofloxacin	Zeniquin, Marbocyl
	Moxifloxacin	Avelox
	Norfloxacin	Noroxin
	Orbifloxacin	Orbax
	Pradofloxacin	Veraflox
Antibacterial, glycopeptide	Vancomycin	Vancocin, Vancoled
Antibacterial, sulfonamide	Sulfachlorpyridazine	Vetisulid
	Sulfadiazine	Combined with trimethoprim in Tribrissen
	Sulfadimethoxine	Albon, Bactrovet, and generic
	Sulfamethazine	Many brands (e.g., Sulmet)
	Sulfamethoxazole	Gantanol
	Sulfaquinoxaline	Sulfa-Nox

*Continued*

Listing of Drugs According to Functional and Therapeutic Classification		
Drug Classification	Drug Name	Brand Name
Antibacterial, tetracycline	Chlortetracycline	Generic, anaplasmosis block, Aureomycin soluble powder, Aureomycin tablets, Aureomycin soluble calf oblets and Calf Scour Bolus, Fermycin
	Doxycycline	Vibramycin, Monodox, Doxy Caps, and generic forms
	Minocycline hydrochloride	Minocin
	Oxytetracycline	Terramycin, Terramycin soluble powder, Terramycin scours tablets; Biomycin, Oxy-Tet, Oxybiotic Oxy 500, Oxy 1000; long-acting formulations include Liquamycin-LA 200, and Biomycin 200
	Tetracycline Tetracycline hydrochloride	Panmycin, Duramycin powder Achromycin V
Antibiotic, aminocyclitol	Spectinomycin dihydrochloride pentahydrate Spectinomycin sulfate tetrahydrate	Spectam, Spectogard, Prospec, Adspec
Anticancer agent	Asparaginase (L-Asparaginase)	Elspar, Asparaginase
	Bleomycin sulfate	Blenoxane
	Busulfan	Myleran
	Carboplatin	Paraplatin
	Chlorambucil	Leukeran
	Cisplatin	Platinol
	Cyclophosphamide	Cytosan, Neosar, CTX
	Cytarabine	Cytosar, Ara-C, Cytosine arabinoside
	Dacarbazine	DTIC
	Doxorubicin hydrochloride	Adriamycin
	Fluorouracil	5-Fluorouracil, Adrucil
	Hydroxyurea	Droxia; Hydrea (Canada)
	Lomustine	CeeNu, CCNU
	Masitinib	Kinavet-CA1
	Melphalan	Alkeran
	Mercaptopurine	Purinethol
	Methotrexate	MTX, Mexate, Folex, Rheumatrex, and generic
	Mitoxantrone hydrochloride	Novantrone
	Paclitaxel	Paccal Vet-CA1
	Plicamycin	Mithracin, Mithramycin
	Streptozocin	Streptozotocin, Zanosar
	Thioguanine	Generic

## Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name	Brand Name
Anticholinergic	Thiotepa	Thioplex and generic
	Toceranib	Palladia
	Vinblastine sulfate	Velban
	Vincristine sulfate	Oncovin, Vincasar
	Atropine sulfate	Many generic brands
	Glycopyrrolate	Robinul-V
	Hyoscyamine	Levsin
	Oxybutynin chloride	Ditropan
	Aminopentamide	Centrine
Anticholinesterase	Pyridostigmine bromide	Mestinon, Regonol
Anticoagulant	Physostigmine	Antilirium
	Neostigmine	Prostigmin, Stiglyn, Neostigmine bromide, Neostigmine methylsulfate
	Dalteparin	Fragmin, LMWH
	Dipyridamole	Persantine, Aggrenox
	Enoxaparin	Lovenox, LMWH
Anticonvulsant	Heparin sodium	Liquaemin, Hepalean (Canada)
	Warfarin sodium	Coumadin and generic
	Bromide	Potassium bromide, sodium bromide
	Clonazepam	Klonopin and generic
	Clorazepate dipotassium	Tranxene
	Felbamate	Felbatol
	Levetiracetam	Keppra
	Lorazepam	Ativan
	Midazolam hydrochloride	Versed
	Oxazepam	Serax
	Phenobarbital	Luminal, Phenobarbitone, and generic
	Phenobarbital sodium	
	Phenytoin	Dilantin
	Phenytoin sodium	
Anticonvulsant, analgesic	Primidone	Mylepsin, Neurosyn (Mysoline in Canada)
	Valproic acid	Depakene (valproic acid); Depakote (divalproex) (Epival is Canadian brand)
	Valproate sodium	
	Zonisamide	Zonegran
	Gabapentin	Neurontin and generic
Anticonvulsant, sedative	Pregabalin	Lyrica
	Diazepam	Valium and generic
	Midazolam hydrochloride	Versed

Continued

Listing of Drugs According to Functional and Therapeutic Classification		
Drug Classification	Drug Name	Brand Name
Antidiarrheal	Bismuth subsalicylate	Pepto Bismol
	Diphenoxylate	Lomotil
	Kaolin and pectin	KaoPectate
	Loperamide	Imodium, and generic
	Mesalamine	Asacol, Mesasal, Pentasa, Mesalazine
	Olsalazine sodium	Dipentum
	Paregoric	Corrective Mixture
	Propantheline bromide	Pro-Banthine
	Sulfasalazine	Azulfidine
Antidote	Charcoal, activated	ActaChar, Charcodote, Liqui-Char, Toxiban
	Deferoxamine mesylate	Desferal
	Dimercaprol	BAL in oil; British anti-lewisite
	Edetate calcium disodium	Calcium disodium versenate, calcium disodium ethylenediaminetetra-acetate (EDTA)
	Flumazenil	Romazicon
	Fomepizole	4-Methylpyrazole, Antizol-Vet, Antizol (human form)
	Leucovorin calcium	Wellcovorin and generic
	Methylene blue 0.1%	Generic; also called New Methylene Blue
	Penicillamine	Cuprimine, Depen
	Pralidoxime chloride	2-PAM, Protopam chloride
	Succimer	Chemet
	Trientine hydrochloride	Syprine
Antiemetic	Aprepitant	Emend
	Dolasetron mesylate	Anzemet
	Dronabinol	Marinol
	Granisetron hydrochloride	Kytril
	Maropitant	Cerenia
	Meclizine	Antivert, Bonine, Meclozine (British name)
	Mirtazapine	Remeron
	Ondansetron hydrochloride	Zofran
	Trimethobenzamide	Tigan and others
Antiemetic, antidiarrheal	Prochlorperazine edisylate	Darbazine
	Prochlorperazine maleate (each with isopropamide iodide)	
Antiemetic, phenothiazine	Chlorpromazine	Thorazine, Largactil

## Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name	Brand Name
	Prochlorperazine edisylate	Compazine
	Prochlorperazine maleate	
	Trifluoperazine hydrochloride	Stelazine
	Triflupromazine hydrochloride	Vesprin, Fluopromazine (old name)
Antiemetic, phenothiazine	Trimepazine tartrate	Temaril, (Panectyl in Canada), Temaril-P (with prednisolone)
	Promethazine hydrochloride	Phenergan
Antihistamine	Propiomazine hydrochloride	Tranvet, Largon
Antiemetic, prokinetic agent	Metoclopramide hydrochloride	Reglan, Maxolon
Antiestrogen	Tamoxifen citrate	Nolvadex
Antifungal	Amphotericin B	Fungizone (traditional formulation) and liposomal forms of Amphotec, ABCD, ABELCET, AmBisome
	Enilconazole	Imaverol, ClinaFarm-EC
	Fluconazole	Diflucan, and generic
	Flucytosine	Ancobon
	Griseofulvin	Microsize - Fulvicin U/F, Grisactin, Grifulvin Ultramicrosize - Fulvicin P/G, GrisPEG
	Itraconazole	Sporanox (Itrafungol for cats is available in Europe)
	Ketoconazole	Nizoral
	Posaconazole	Noxafil
	Terbinafine hydrochloride	Lamisil
	Voriconazole	Vfend
Antifungal, expectorant	Potassium iodide	Quadrinal
Antihistamine	Cetirizine hydrochloride	Zyrtec
	Chlorpheniramine maleate	Chlortrimeton, Phenetron, and others
	Clemastine fumarate	Tavist, Contac 12 hr allergy, and generic
	Cyproheptadine hydrochloride	Periactin
	Dimenhhydrinate	Dramamine (Gravol in Canada)
	Diphenhydramine hydrochloride	Benadryl
	Hydroxyzine	Atarax
	Tripelennamine citrate	Pelamine, PBZ

Continued



Listing of Drugs According to Functional and Therapeutic Classification		
Drug Classification	Drug Name	Brand Name
Antihypercalce-mic agent	Alendronate	Fosamax
	Clodronate disodium	Osphos
	Etidronate disodium	Didronel
	Pamidronate disodium	Aredia
	Tiludronate	Tildren, Skelid
	Zoledronate	Zometa
Antihyperglyce-mic agent	Metformin	Glucophage
	Glipizide	Glucotrol
	Glyburide	Diabeta, Micronase, Glynase, Glibenclamide (British name)
Antihyperlipid-emic agent	Gemfibrozil	Lopid
Anti-inflammatory agent, anti-pruritic	Oclacitinib	Apoquel
	Allopurinol	Lopurin, Zyloprim, Allopur (Europe)
Anti-inflamma-tory agent	Colchicine	Generic
	Dimethyl Sulfoxide (DMSO)	DMSO, Domoso
	Pentoxifylline	Trental, oxpentifylline
Anti-inflamma-tory, cortico-steroid	Niacinamide	Nicotinamide, vitamin B <sub>3</sub>
	Budesonide	Entocort
	Betamethasone	Celestone, betamethasone acetate, betamethasone benzoate
	Desoxycorticosterone pivalate	Percorten-V, DOCP, or DOCA pivalate
	Dexamethasone	Azium solution in polyethylene glycol; Dexaject; Dex-A-Vet, Decadron, Dexasone, and generic
	Dexamethasone sodium phosphate	Sodium phosphate forms include Dexaject SP, Dexavet, and Dexasone Tablets include Decadron and generic
	Flumethasone	Flucort
	Hydrocortisone	Hydrocortisone: Cortef and generic Hydrocortisone sodium succinate: Solu-Cortef
	Isoflupredone acetate	Predef 2X
	Methylprednisolone	Methylprednisolone: Medrol Methylprednisolone acetate: Depo-Medrol Methylprednisolone sodium succinate: Solu-Medrol
	Prednisolone sodium succinate	Solu-Delta-Cortef
	Prednisolone	Delta-cortef, PrednisTab, and generic tablets
	Prednisolone acetate	
	Prednisone	Deltasone and generic; Meticorten for injection

**Listing of Drugs According to Functional and Therapeutic Classification**

<b>Drug Classification</b>	<b>Drug Name</b>	<b>Brand Name</b>
Antimythasthenic	Triamcinolone acetonide	Vetalog, Triamtabs, Aristocort
	Triamcinolone hexacetonide	Triamcinolone acetonide: Vetalog
	Triamcinolone diacetate	
	Edrophonium chloride	Tensilon and others
	Pyridostigmine bromide	Mestinon, Regonol
Antibesity	Physostigmine	Antilirium
	Neostigmine	Prostigmin, Stiglyn
	Dirlotapide	Slentrol
Antiparasitic	Mitratapide	Yarvitan
	Albendazole	Valbazen
	Afoxolaner	NexGuard
	Amitraz	Mitaban
	Amprolium	Amprol, Corid
	Bunamidine hydrochloride	Scolaban
	Dichlorvos	Task, Dichlorovos, Atgard, DDVP, Verdisol, Equigard
	Diethylcarbamazine citrate	Caricide, Filaribits, Nemacide
	Dithiazanine Iodide	Dizan
	Doramectin	Dectomax
	Epsiprantel	Cestex
	Febantel	Rintal, Vercom
	Fenbendazole	Panacur, SafeGuard
	Furazolidone	Furoxone
	Ivermectin	Heartguard, Ivomec, Eqvalan liquid, Equimectrin, IverEase, Zimecterin, Privermectin, Ultramectin, Ivercide, Ivercare, Ivermax
	Ivermectin and Praziquantel	Equimax
	Levamisole hydrochloride	Levasole, Ripercol, Tramisol, Ergamisol
	Lufenuron	Program
	Lufenuron and milbemycin oxime	Sentinel tablets and Flavor Tabs
	Mebendazole	Telmintic, Telmin, Vermox (human drug)
	Melarsomine	Immiticide
	Metaflumizone	ProMeris
	Milbemycin oxime	Interceptor, Interceptor Flavor Tabs, and SafeHeart; milbemycin also is an ingredient in Sentinel
	Moxidectin	ProHeart (canine) Quest (equine) Cydectin (bovine)

*Continued*

Listing of Drugs According to Functional and Therapeutic Classification		
Drug Classification	Drug Name	Brand Name
Antiparasitic agent	Nitenpyram	Capstar
	Oxfendazole	Benzelmin, Synanthic
	Oxibendazole	Anthelcide EQ
	Paromomycin sulfate	Humatin
	Piperazine	Pipa-Tabs and many generic forms
	Praziquantel	Droncit, Drontal (combination with febantel)
	Pyrantel pamoate	Nemex, Strongid, Priex, Pyran, Pyr-A-Pam
	Pyrantel tartrate	
	Quinacrine hydrochloride	Atabrine (No longer available in US)
	Selamectin	Revolution
	Spinosad	Comfortis
	Thenium closylate	Canopar
	Thiabendazole	Omnizole, Equizole, TBZ, Thibenzole
	Thiacetarsamide sodium	Caparsolate
	Clopidogrel	Plavix
Antiprotozoal	Atovaquone	Meproon
	Diclazuril	Clincox
	Imidocarb hydrochloride	Imizol
	Nitazoxanide	Navigator (horses) Alinia (human)
Antifungal agent	Ponazuril	Marquis
	Pyrimethamine and Sulfadiazine	ReBalance
	Tinidazole	Tindamax
	Toltrazuril	Baycox
	N-butylscopolammonium bromide (butylscopolamine bromide)	Buscopan
Antithyroid agent	Carbimazole	Neomercazole
	Iopanoic acid	Generic
	Iodate	Calcium iodate
Antitussive	Methimazole	Tapazole
	Propylthiouracil	Generic, Propyl-Thyracil, PTU
	Hydrocodone bitartrate and homatropine	Hycodan
Antidiarrheal agent	Dextromethorphan	Benylin and others
	Misoprostol	Cytotec
	Sucralfate	Carafate (Sulcrate in Canada)

**Listing of Drugs According to Functional and Therapeutic Classification**

<b>Drug Classification</b>	<b>Drug Name</b>	<b>Brand Name</b>
Antiulcer agent, H <sub>2</sub> -blocker	Cimetidine hydrochloride	Tagamet (OTC and prescription)
	Famotidine	Pepcid
	Nizatidine	Axid
	Ranitidine hydrochloride	Zantac
Antiulcer agent, proton pump inhibitor	Esomeprazole	Nexium
	Omeprazole	Prilosec (formerly Losec), human formulation GastroGard and UlcerGard are equine formulations
	Pantoprazole	Protonix
Antiviral	Acyclovir	Zovirax
	Famciclovir	Famvir
	Lysine (L-Lysine)	Enisyl-F
	Valacyclovir	Valtrex
	Zidovudine	Retrovir
Antiviral, analgesic	Amantadine	Symmetrel
Behavior-modifying drug	Buspirone hydrochloride	BuSpar
	Trazodone	Desyrel
	Doxepin	Sinequan
Behavior-modifying drug, tricyclic antidepressant	Amitriptyline hydrochloride	Elavil and generic brands
	Clomipramine hydrochloride	Clomicalm (veterinary); Anafranil (human)
	Imipramine hydrochloride	Tofranil
Behavior-modifying drug, selective serotonin reuptake inhibitor	Fluoxetine hydrochloride	Prozac
	Paroxetine	Paxil
Beta-agonist	Isoproterenol hydrochloride	Isuprel, isoprenaline hydrochloride
Beta-blocker	Atenolol	Tenormin
	Bisoprolol	Zebeta
	Esmolol hydrochloride	Brevibloc
	Metoprolol tartrate	Lopressor
	Propranolol hydrochloride	Inderal and generic
	Sotalol hydrochloride	Betapace

*Continued*

Listing of Drugs According to Functional and Therapeutic Classification		
Drug Classification	Drug Name	Brand Name
Bronchodilator	Aminophylline	Generic forms
	Oxtriphylline	Choledyl-SA
	Theophylline	Many brands and generic Theophylline sustained-release is by Inwood Laboratories: Theo-Dur, Slo-bid, Gyrocaps
Bronchodilator, beta-agonist	Albuterol sulfate	Proventil, Ventolin Also known as Salbutamol in other countries Torpex Equine Inhaler
	Clenbuterol	Ventipulmin
	Fluticasone	Flovent, Advair
	Metaproterenol sulfate	Alupent, Metaprel, Orciprenaline Sulphate
	Terbutaline sulfate	Brethine, Bricanyl
	Zilpaterol	Zilmax
Calcium supplement	Calcitriol	Rocaltrol, Calcijex
	Calcium carbonate	Many brands available: Titalac, Calci-mix, Liqui-cal, Maalox, Tums
	Calcium chloride	Generic
	Calcium citrate	Citracal (OTC)
	Calcium gluconate and Calcium borogluconate	Kalcinate, Calcium borogluconate, AmVet, Cal-Nate, and generic
	Calcium lactate	Generic; many brands available
Cardiac inotropic agent	Digitoxin	Crystodigin
	Digoxin	Lanoxin, Cardoxin
	Dobutamine hydrochloride	Dobutrex
Cardiac inotropic agent, vasodilator	Pimobendan	Vetmedin
Cardiac inotropic agent, beta-agonist	Dopamine hydrochloride	Intropin
Cholinergic	Bethanechol chloride	Urecholine
Corticosteroid, replacement hormone	Fludrocortisone acetate	Florinef
Dermatologic agent	Isotretinoin	Accutane
Diuretic	Acetazolamide	Diamox
	Chlorothiazide	Diuril
	Dichlorphenamide	Daranide
	Furosemide	Lasix
	Hydrochlorothiazide	HydroDiuril and generic
	Mannitol	Osmitol

**Listing of Drugs According to Functional and Therapeutic Classification**

<b>Drug Classification</b>	<b>Drug Name</b>	<b>Brand Name</b>
Diuretic, laxative	Methazolamide	Nepta-zane
	Spironolactone	Aldactone
	Triamterene	Dyrenium
	Glycerin	Generic
Dopamine agonist	Bromocriptine mesylate	Parlodel
	Levodopa	Larodopa, L-dopa
	Pergolide	Permax
	Pergolide mesylate	
	Selegiline hydrochloride	Anipryl (also known as deprenyl and l-deprenyl); human dose form is Eldepryl
Emetic	Apomorphine hydrochloride	Generic
Expectorant, muscle relaxant	Ipecac	Ipecac, Syrup of Ipecac
	Guaifenesin	Glyceril guaiacolate, Guaiphenesin, Gecolate, Guailaxin, Glycotuss, Hytuss, Glytuss, Fenesin, Humabid LA
Fluid replacement	Dextran	Dextran 70 Gentran-70
	Dextrose solution	D5W
	Hydroxyethyl starch	HES, Tetrastarch, Hespan
	Lactated Ringer's solution	LRS and other names
	Pentastarch	Pentaspan
	Ringer's solution	Generic
	Sodium chloride 0.9%	Generic, normal saline
	Sodium chloride 7.2%	Hypertonic saline, HSS
	S-adenosylmethionine (SAMe)	Denosyl, SAME
Hepatic protectant	Silymarin	Silybin, Marin, milk thistle
Hormone	Colony-stimulating factors	Leukine, Neupogen
	Corticotropin	Acthar
	Cosyntropin	Cortrosyn, Synthetic ACTH, Tetracosactrin, Tetracosactide
	Danazol	Danocrine
	Desmopressin acetate	DDAVP
	Diethylstilbestrol	DES
	Epoetin alpha (erythropoietin)	Epogen, epoetin alfa, "EPO," (r-HuEPO), erythropoietin
	Darbepoetin alfa	Aranesp
	Estradiol cypionate	ECP, Depo-Estradiol
	Estriol	Incurin

*Continued*

Listing of Drugs According to Functional and Therapeutic Classification		
Drug Classification	Drug Name	Brand Name
Hormone	Gonadorelin hydrochloride, Gonadorelin diacetate tetrahydrate	Factrel, Fertagyl, Cystolelin, Fertelin, OvaCyst, GnRh, LHRH
	Gonadotropin, chorionic	Profasi, Pregnyl, A.P.L.
	Growth hormone	Somatrem and Somatropin; brand names include Protropin, Humatrope, Nutropin
	Insulin	Lente insulin, Ultralente insulin, Regular insulin, NPH insulin, Protamine zinc insulin (PZI) Human insulin is Humulin (discontinued) Vetsulin is porcine insulin zinc suspension (veterinary) PZI Vet (veterinary protamine zinc insulin)
	Levothyroxine sodium	T4, Soloxine, Thyro-Tabs, Synthroid, ThyroMed; equine powders include Equisyn-T4, Levo-Powder, Thyroid Powder, Thyro-L
	Liothyronine sodium	Cytomel
	Medroxyprogesterone acetate	Depo-Provera (injection); Provera (tablets); Cycrin tablets
	Megestrol acetate	Ovaban, Megace
	Mibolerone	Cheque-drops
	Testosterone	Testosterone cypionate ester: Andro-Cyp, Andronate, Depo-Testosterone and other forms Testosterone propionate ester: Testex, (Malogen in Canada)
	Urofollitropin	Metrodin, FSH, Fertinex
	Vasopressin	Pitressin
	Finasteride	Proscar
	Hormone antagonist	
	Hormone, anabolic agent	
Hormone, anabolic agent	Boldenone Undecylenate	Equipoise
	Methyltestosterone	Android
	Nandrolone decanoate	Deca-Durabolin
	Oxymetholone	Anadrol
	Stanozolol	Winstrol-V
Hormone, progestin	Altrenogest	ReguMate, Matrix
	Megestrol acetate	Ovaban, Megace
Hormone, thyroid	Thyroid-releasing hormone	TRH
	Thyrotropin	Thytropar, Thyrogen, TSH
Hormone, labor induction	Oxytocin	Pitocin, Syntocinon (nasal solution), and generic
Immunostimulant	Interferon	Virbagen Omega
	Lithium carbonate	Lithotabs
Immunosuppressive agent	Auranofin	Ridaura

## Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name	Brand Name
Iodine supplement	Aurothioglucose	Solganal
	Azathioprine	Imuran
	Cyclosporine	Atopica (veterinary); Neoral (human); Sandimmune; Optimmune (ophthalmic); Gengraf, and generic formulations Other name for cyclosporine is cyclosporin A
	Gold sodium thioma- late	Myochrysine
	Leflunomide	Arava
	Mycophenolate	CellCept
	Tacrolimus	Protopic, also known as FK506
	Iodide	Potassium Iodide
	Sodium iodide (20%)	Iodopen
	Laxative	
Laxative	Bisacodyl	Dulcolax
	Cascara sagrada	Nature's Remedy and other brands
	Castor oil	Generic
	Docusate	Docusate calcium: Surfak, Doxidan Docusate sodium: DSS, Colace, Doxan Many OTC brands are available
	Lactulose	Chronulac
	Magnesium citrate	Citroma, CitroNesia (Citro-Mag in Canada)
	Magnesium hydroxide	Milk of Magnesia, Carmilax, Magnalax
	Mineral oil	Generic
	Polyethylene glycol electrolyte solution	Golytely, PEG, Colyte, Co-Lav
	Psyllium	Metamucil and others
Laxative, anti- arrhythmic	Senna	Senokot
	Ursodiol	Actigall, Ursodeoxycholic acid
	Ursodeoxycholic Acid	
	Magnesium sulfate	Epsom salts
	Local anes- thetic	
	Bupivacaine hydrochloride	Marcaine and generic
	Mepivacaine	Carbocaine-V
	Local anes- thetic, antiar- rhythmic	
	Lidocaine hydrochloride	Xylocaine
	Mucolytic, antidote	
Muscle relaxant	Acetylcysteine	Mucomyst, Acetadote
	Atracurium besylate	Tracrium
	Dantrolene sodium	Dantrium
	Methocarbamol	Robaxin-V
	Pancuronium bromide	Pavulon
	Nutritional supplement	
	Ferrous sulfate	Ferospace and other generic OTC brands available

Continued



Listing of Drugs According to Functional and Therapeutic Classification		
Drug Classification	Drug Name	Brand Name
Opioid Antagonist	Iron Dextran	AmTech Iron Dextran, Ferrodex, HemaJect
	MCT oil	MCT oil (many sources), medium chain triglycerides
	Taurine	Generic
	Zinc	Zinc (various forms)
	Naloxone hydrochloride	Narcan, Trexonil
Pancreatic enzyme	Naltrexone	Trexan
Potassium supplement	Pancrelipase	Viokase, Pancrezyme, Cotazym, Creon, Pancoate, Pancrease, Ultrase
	Potassium chloride	Generic
Prokinetic agent	Potassium gluconate	Kaon, Tumil-K, generic
	Potassium phosphate	K-Phos, Neutra-Phos-K, and generic
Prostaglandin	Cisapride	Propulsid (Propulsid in Canada)
	Domperidone	Motilium, Equidone
	Methylnaltrexone	Relistor
	Metoclopramide	Reglan
	Tagaserod	Zelnorm
	Cloprostamol	Estrumate, estroPlan
Respiratory stimulant	Dinoprost tromethamine	Lutalyse, Dinoprost, Prostin F2 alpha, ProstaMate, Prostaglandin F2alpha, PGF2alpha
	Prostaglandin F-2 alpha	Lutalyse, Dinoprost, PG-F2 alpha
Sedative	Doxapram hydrochloride	Dopram
Tranquilizer, benzodiazepine	Zolpidem	Ambien
Tranquilizer, Phenothiazine.	Alprazolam	Xanax, Niravam
Vasodilator	Acepromazine maleate	ACE, Aceproject, Aceprotabs, Atravet, Promace; It sometimes appears as a nickname of acetylpromazine.
	Hydralazine hydrochloride	Apresoline
	Irbesartan	Avapro
	Isosorbide dinitrate	Isosorbide dinitrate: Isordil, Isorbid, Sorbitrate
	Isosorbide mononitrate	Isosorbide mononitrate: Monoket
	Isoxsuprine	Vasodilan, and generic
	Nitroglycerin	Nitrol, Nitro-bid, Nitrostat
	Nitroprusside (Sodium nitroprusside)	Nitropress

## Listing of Drugs According to Functional and Therapeutic Classification

Drug Classification	Drug Name	Brand Name
Vasodilator, ACE inhibitor	Phenoxybenzamine hydrochloride	Dibenzyline
	Phentolamine mesylate	Regitine (Rogitine in Canada)
	Prazosin	Minipress
	Sildenafil	Viagra
	Benazepril hydrochloride	Lotensin (human preparation), Fortekor (veterinary formulation)
	Captopril	Capoten
	Enalapril maleate	Enacard (veterinary), Vasotec (human)
	Lisinopril	Prinivil, Zestril
	Ramipril	Vasotop
Vasodilator, angiotensin receptor blocker	Trandolapril	Mavik
	Losartan	Cozaar
Vasodilator, calcium channel blocker	Telmisartan	Micardis
	Amlodipine besylate	Norvasc
Vasopressor	Nifedipine	Adalat, Procardia
	Arginine vasopressin	Vasopressin, Pitressin
	Methoxamine	Vasoxyl
Vitamin	Phenylephrine hydrochloride	Neo-synephrine
	Ascorbic acid	Vitamin C, sodium ascorbate; there are many brand names available
	Cyanocobalamin	Vitamin B <sub>12</sub>
	Dihydrotachysterol	Hytakerol, DHT
	Ergocalciferol	Calciferol, Drisdol
	Phytonadione	Aquamephyton (injection), Mephyton (tablets), Veta-K1 (capsules), vitamin K1, Phylloquinone; Phytomenadione
	Riboflavin	Vitamin B <sub>2</sub>
	Thiamine hydrochloride	Vitamin B <sub>1</sub> , Bewon, and others
	Vitamin A	Retinol, Aquasol-A, Vitamin AD, vitamin A and D
	Vitamin E	Tocopherol, alpha-tocopherol, Aquasol E, and generic
	Vitamin K	Aquamephyton (injection), Mephyton (tablets); Veta-K1 (capsules), Veda-K1 (oral and injectable), vitamin K1, Phylloquinone, Phytomenadione



## Acepromazine Maleate

ayss-proe'meh-zeen mal'ee-ate

**Trade and other names:** ACE, AceproJect, AceproTabs, Atravet, and PromAce; it sometimes is called acetylpromazine

**Functional classification:** Tranquilizer, phenothiazine tranquilizer

### Pharmacology and Mechanism of Action

Phenothiazine tranquilizer and sedative. Acepromazine inhibits central dopaminergic receptors to produce sedation and tranquilization. Acepromazine also has antimuscarinic action and blocks norepinephrine at adrenergic receptors (e.g., alpha-receptors). Because of the blockade of alpha-receptors on vascular smooth muscle, it also produces vasodilation. When administered as an anesthetic adjunct, it may produce a decrease in vascular resistance and lower blood pressure, but usually does not decrease cardiac output. In horses, IV administration significantly increases the blood flow through digital arteries and laminae.

### Indications and Clinical Uses

Acepromazine is used as a sedative, a tranquilizer, a preanesthetic, and an anesthetic adjunct. In small animals, duration of sedation can occur within 10 minutes and have a 4-6 hour duration. In small animals, acepromazine can produce antiemetic effects. For some indications, the administration also produces vasodilation. In horses for treatment of laminitis, it has increased the arterial digital blood flow after a dose of 0.02-0.06 mg/kg.

### Precautionary Information

#### Adverse Reactions and Side Effects

Sedation and ataxia are common side effects. Extrapyrimal effects (involuntary muscle movements), twitching, dystonia, or parkinsonlike effects are rare but are possible with the administration of phenothiazines to animals. Phenothiazines may produce excessive vagal tone in some animals. This may be especially prominent in brachycephalic breeds. Administration of atropine may be used to treat the signs of high vagal tone. Because of alpha-adrenergic antagonism, hypotension is possible in animals. In horses, persistent penile prolapse has been reported from use. This effect in horses is unpredictable. Some resources indicate that it is dose-dependent with increased likelihood as the dose is increased from 0.01 mg/kg to 0.1 mg/kg IV. The duration of penile prolapse in horses may be as long as 4 hours with high doses. In rare cases, penile prolapse can lead to permanent paraphimosis. The mechanism is unknown but may be caused by the alpha-adrenergic blockade induced by acepromazine.

#### Contraindications and Precautions

It is often stated in veterinary literature that acepromazine may increase risk of seizures in animals and it should be administered cautiously in animals that are prone to seizures. However, a risk of seizures in animals from administration of acepromazine may not be as great as was once thought. Seizures were not reported to be a clinical problem in retrospective studies of patients who had them. Seizures were not reported in studies in which animals prone to seizures were anesthetized and administered acepromazine as an anesthetic adjunct.

Do not use in animals that have problems with dystonia or that have had extrapyramidal effects from use of phenothiazines.

## 2 Acepromazine Maleate

Phenothiazines can cause hypotension (via alpha-receptor blockade); therefore use cautiously with other hypotensive drugs or in conditions that may exacerbate hypotension. When administered as a pre-anesthetic to dogs (0.05 mg/kg) it induces moderate hypotension, but does not affect cardiac output significantly.

In pregnancy it produced only minor reduction in blood flow and oxygen delivery to the fetus when used in late pregnancy in cows.

### Drug Interactions

Acepromazine may potentiate other drugs that cause vasodilation. Acepromazine may increase the risk of seizures if administered with other drugs that lower seizure threshold, but this may not be as much of a risk as was once thought.

Acepromazine has been used to sedate dogs for glucose tolerance testing (0.1 mg/kg), without adversely affecting the results.

### Instructions for Use

Acepromazine can be administered PO, IV, or IM. When used with general anesthetics, lower doses of general anesthetics can be used, especially when administering barbiturates and inhalant anesthetics. Clinical signs from acepromazine administration are most prominent during the first 3-4 hours after administration, but may persist for 7 hours.

### Patient Monitoring and Laboratory Tests

Monitor blood pressure in animals susceptible to hypotension. Acepromazine does not affect adrenal function testing in dogs.

### Formulations

- Acepromazine is available in 5-, 10-, and 25-mg tablets and in a 10-mg/mL injection.
- Acepromazine oral granules and powder are available in Canada.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been investigated.

### Small Animal Dosage

#### Dogs

- 0.025-0.1 mg/kg IM, IV, or SQ in a single dose (most common is 0.025 mg/kg). Do not exceed 3 mg total in dogs.
- Sedation: 0.5-2.2 mg/kg q6-8h PO.

#### Cats

- 0.025-0.1 mg/kg IM, IV, or SQ in a single dose.
- Sedation: 1.1-2.2 mg/kg q6-8h PO.

### Large Animal Dosage

#### Horses

- 0.04-0.1 mg/kg IM, q 6-12h, but frequent dosing is not recommended, and an interval of 36-48 hours between doses is recommended. For perioperative use, 0.01-0.05 mg/kg, IM, SQ, or IV.

#### Cattle

- 0.13-0.26 mg/kg PO, 0.03-0.1 mg/kg IM, or 0.01-0.02 mg/kg IV.

#### Pigs

- Adult: 0.03-0.2 mg/kg IV, IM, SQ (single dose).

### Regulatory Information

Withdrawal times: There are no withdrawal times established in the US. It has been estimated that for extralabel use, establish a withdrawal time of at least 7 days for meat and 48 hours for milk.

Canada: 7 days for meat; 48 hours for milk.

RCI Classification: 3

## Acetaminophen

ah-seet-ah-mee'noe-fen

**Trade and other names:** Tylenol and generic brands. Known outside the United States as paracetamol.

**Functional classification:** Analgesic

### Pharmacology and Mechanism of Action

Analgesic drug. Exact mechanism of action is not known; however, acetaminophen probably inhibits centrally mediated pain transmission. The centrally mediated analgesia may occur via inhibition of COX-3, a variant of COX-1 found in the central nervous system (CNS). Other evidence indicates that acetaminophen may inhibit prostaglandins in some cells and tissue in which low concentrations of arachidonic acid are present. The site of acetaminophen action may be the peroxidase enzyme component of prostaglandin H<sub>2</sub> synthase. Therefore cyclo-oxygenase enzyme (COX) inhibition may occur at site-specific tissues, sparing the gastrointestinal (GI) mucosa, platelets, and kidneys but acting centrally. Other evidence suggests that acetaminophen can stimulate inhibitory pain pathways mediated by serotonin (5-HT<sub>3</sub>). This evidence suggests that acetaminophen may directly activate serotonin receptors.

In canine studies it has not produced anti-inflammatory action, but has been effective as an analgesic agent.

### Indications and Clinical Uses

Acetaminophen is used as an analgesic and for pain control in dogs. Do not use in cats. It is considered relatively weak as an analgesic. Often used in combination with an opiate (e.g., codeine). Acetaminophen has been used in experimental animals to measure the rate of stomach or abomasal emptying by documenting the appearance of the drug in plasma.

### Precautionary Information

#### Adverse Reactions and Side Effects

Acetaminophen is well tolerated in dogs at doses listed; however, high doses have caused liver toxicity. It causes severe toxicosis in cats because of their inability to excrete metabolites. Acetaminophen relies on conjugation with glutathione for excretion and deficiencies in glutathione can lead to toxicity. Clinical signs of toxicity include methemoglobinemia, acute hepatic toxicosis, swelling of paws, and Heinz body anemia.

#### Contraindications and Precautions

Do not administer to cats. In people, toxic episodes are more likely when administered with drugs that alter the activity of hepatic drug enzymes. Such a reaction also is possible in animals.

In cats, treatment of intoxication requires prompt treatment with acetylcysteine (see monograph for acetylcysteine) and monitoring.

#### Drug Interactions

In people, other drugs (especially alcohol) will increase risk of hepatotoxicosis. It is not known if other drugs increase this risk in animals.

## 4 Acetaminophen 1 Codeine

### Instructions for Use

Many nonprescription (over-the-counter or OTC) formulations are available. Acetaminophen with codeine may have greater analgesic efficacy in some animals. See other entries for formulations that contain codeine.

### Patient Monitoring and Laboratory Tests

Monitor liver enzyme levels periodically to look for evidence of hepatotoxicity. In cats that have received acetaminophen, there is a high risk of toxicity, and careful monitoring of liver enzymes and blood cell parameters is needed. Many human hospitals and some diagnostic laboratories can measure acetaminophen concentrations in plasma. In people, treatment is initiated if plasma/serum concentrations are above 200 mcg/mL 4 hours after ingestion.

### Formulations

- Acetaminophen is available in 120-, 160-, 325-, and 500-mg tablets.

### Stability and Storage

Acetaminophen is stable in aqueous solutions. Maximum stability is at pH of 5-7.

### Small Animal Dosage

#### Dogs

- 15 mg/kg q8h PO.

#### Cats

- Contraindicated.

### Large Animal Dosage

#### Calves

- 50 mg/kg PO, followed by 30 mg/kg PO q6h.
- No other doses have been reported for large animals.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

Racing Commissioners International (RCI) Classification: 4

## Acetaminophen + Codeine

ah-seet-ah-mee'noe-fen + koe'deen

**Trade and other names:** Tylenol with codeine and many generic brands

**Functional classification:** Analgesic, opioid

### Pharmacology and Mechanism of Action

Analgesic agent. Exact mechanism of action for acetaminophen is not known; however, as discussed previously, a centrally mediated mechanism is likely, either via inhibition of central prostaglandin synthesis or effects on serotonergic inhibitory pain pathways. In this formulation, the opiate codeine is added to enhance analgesia. Effects of codeine are not established in animals. Systemic absorption of codeine from oral administration is small in dogs, and codeine may play only a minor role in analgesia.

### Indications and Clinical Uses

Acetaminophen + codeine is used for analgesia in dogs (e.g., postoperative use). Codeine or codeine with acetaminophen is indicated for treatment of moderate pain.

Codeine formulations have also been used as an antitussive. Despite the widespread use of codeine in humans, the efficacy in animals for its antitussive use or analgesic use has not been established.

Oral absorption of codeine in dogs is low. Because codeine is converted to morphine (10% of dose) for its activity and the duration of morphine is short in dogs, the clinical effectiveness of codeine in dogs may be questionable.

### Precautionary Information

#### Adverse Reactions and Side Effects

Acetaminophen + codeine is well tolerated in dogs at doses listed; however, high doses have caused liver toxicity.

#### Contraindications and Precautions

Do not administer to cats because acetaminophen is known to be toxic to cats. Codeine is a Schedule II controlled substance.

#### Drug Interactions

In people, other drugs (especially alcohol) will increase risk of hepatotoxicity. It is not known if other drugs increase this risk in animals, but consider this possibility when administering other drugs that may affect hepatic metabolism.

### Instructions for Use

Many generic preparations are available. Consider that other ingredients may be present in some combination tablets (e.g., ibuprofen or caffeine).

### Patient Monitoring and Laboratory Tests

Monitor liver enzyme levels periodically to look for evidence of hepatotoxicity caused by acetaminophen.

### Formulations

- Acetaminophen + codeine is available in oral solution and tablets. A variety of formulations are available (e.g., 300 mg acetaminophen plus 15, 30, or 60 mg codeine).

### Stability and Storage

Acetaminophen is stable in aqueous solutions. Maximum stability is at pH of 5-7.

### Small Animal Dosage

#### Dogs

Follow dosing recommendations for codeine. Administer deliver doses of codeine equivalent to 0.5-1.0 mg/kg q4-6h PO.

#### Cats

- Contraindicated.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Acetaminophen + codeine is a Schedule III drug controlled by the Drug Enforcement Agency (DEA). Do not administer to animals intended for food.



## Acetazolamide

ah-seet-ah-zole'a-mide

**Trade and other names:** Diamox, Vetamox (veterinary formulation)

**Functional classification:** Diuretic

### Pharmacology and Mechanism of Action

Carbonic anhydrase inhibitor. Acetazolamide, like other carbonic anhydrase inhibitors, produces diuresis through inhibition of the uptake of bicarbonate in proximal renal tubules via enzyme inhibition. This action results in loss of bicarbonate in the urine and diuresis. The action of carbonic anhydrase inhibitors results in urine loss of bicarbonate, alkaline urine, and water loss.

### Indications and Clinical Uses

Acetazolamide is rarely used as a diuretic any longer. More potent and more effective diuretic drugs are available, such as the loop diuretics (furosemide).

Acetazolamide, like other carbonic anhydrase inhibitors, is used primarily to lower intraocular pressure in animals with glaucoma. Methazolamide is used more often than acetazolamide for this purpose, and other treatment regimens are now used more often than carbonic anhydrase inhibitors.

Acetazolamide also is sometimes used to produce more alkaline urine for management of some urinary calculi.

### Precautionary Information

#### Adverse Reactions and Side Effects

Acetazolamide can potentially produce hypokalemia in some patients. Significant bicarbonate loss can occur with repeated administration. In dogs, a respiratory reaction has been observed, which is attributed to respiratory acidosis.

#### Contraindications and Precautions

Do not use in patients with acidemia. Use cautiously in any animal sensitive to sulfonamides.

#### Drug Interactions

Acetazolamide will produce alkaline urine, which may affect clearance of some drugs. Alkaline urine may potentiate the effects of some antibacterial drugs (e.g., macrolides and quinolones).

### Instructions for Use

Acetazolamide, in combination with other agents, is usually used to decrease intraocular pressure in the treatment of glaucoma. Acetazolamide has been used to produce alkaline urine to prevent formation of some urinary calculi. However, unless there is supplementation with bicarbonate, the urine alkalinization will not be sustained with repeated administration.

### Patient Monitoring and Laboratory Tests

Monitor patient's ocular pressure when used to treat glaucoma.

### Formulations

- Acetazolamide is available in 125- and 250-mg tablets, and a soluble powder for dogs.

### Stability and Storage

Stable if stored in tight containers. Compounded solutions are stable at least 60 days.

## Small Animal Dosage

### Dogs

Note: the approved veterinary formulation lists a dose of 10-30 mg/kg for glaucoma and diuretic uses.

- Glaucoma: 5-10 mg/kg q8-12h PO.
- Other diuretic uses: 4-8 mg/kg q8-12h PO.

### Cats

- 7 mg/kg, q8h, PO.

## Large Animal Dosage

### Horses

- Treatment of Hyperkalemic Periodic Paralysis (HYPP), 2-4 mg/kg PO, every 8 to 12 hours.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Acetylcysteine

ah-see-til-sis'tay-een

**Trade and other names:** Mucomyst and Acetadote; also referred to as N-acetylcysteine

**Functional classification:** Mucolytic, antidote

## Pharmacology and Mechanism of Action

Acetylcysteine decreases viscosity of secretions and is used as a mucolytic agent in eyes and in bronchial nebulizing solutions. Acetylcysteine is a sulfhydryl compound and acts to increase synthesis of glutathione in the liver. Glutathione subsequently acts as an antioxidant and facilitates conjugation to toxic metabolites, particularly the toxic metabolites of acetaminophen. The antioxidant effects also have been used to treat conditions associated with oxidative stress. The pharmacokinetics have been studied in cats. It has a half-life of approximately 1.5 hours and oral absorption of 33%. The clearance is faster than in humans.

## Indications and Clinical Uses

As a donator of the sulfhydryl group, it is used as an antidote for intoxications (e.g., acetaminophen toxicosis in cats). When treating poisoning, it is important that acetylcysteine be administered as soon as possible for optimum effectiveness. Acetylcysteine also has been used to prevent contrast medium-induced nephropathy. Acetylcysteine has been used as a treatment of oxidative stress because it is a scavenger of hydroxyl radicals and hypochlorous acid. It also has been used to treat heavy metal toxicosis when administered with chelating agents. Acetylcysteine will reduce cerebral edema.

## Precautionary Information

### Adverse Reactions and Side Effects

Allergic reactions have been reported in people, which resemble anaphylactic reactions when it is given IV. These reactions manifest as skin reactions, bronchospasm, tachycardia, and hypotension. Vomiting has been observed in cats, but this also may be caused by the toxicant (acetaminophen). When delivered via aerosol to the airways of cats, it increased airway resistance and could worsen airway disease in cats.

**Contraindications and Precautions**

Acetylcysteine may cause sensitization with prolonged topical administration. It may react with certain materials in nebulizing equipment. Avoid delivering via aerosol to the airways of cats because it might worsen clinical airway disease.

**Drug Interactions**

Acetylcysteine acts to donate sulfhydryl groups and may facilitate drug conjugation.

**Instructions for Use**

Available as an agent for decreasing viscosity of respiratory secretions, but most common use is as a treatment for intoxications. In cats, acetylcysteine is used to treat acetaminophen toxicosis. When treating an intoxication, doses are listed here, but consult a poison control center for specific guidelines. The doses used in cats (and listed in the dosing section) are extrapolated from dosages used in humans for treatment of intoxication. However, pharmacokinetics are different in cats (shorter half-life and faster clearance) and higher doses may be needed. For treatment of oxidative stress, constant-rate infusions have been used in which 50 mg/kg is diluted 1:4 in saline solutions and administered IV over the course of 1 hour.

**Patient Monitoring and Laboratory Tests**

When used to treat acetaminophen toxicity, monitor complete blood count (CBC) and liver enzyme concentrations.

**Formulations**

- Acetylcysteine is available in a 20% solution (200 mg/mL).

**Stability and Storage**

Acetylcysteine is unstable in air and easily oxidizes. It should be protected from light. Discard open vials after 96 hours.

**Small Animal Dosage****Dogs and Cats**

- Antidote: 140 mg/kg (loading dose), then 70 mg/kg q4h IV or PO for 5 doses.
- Eye solution: 2% solution topically q2h.
- To prevent contrast-medium nephropathy: 17 mg/kg IV bolus, followed by 17 mg/kg every 12 hours for 48 hours.
- Constant-rate infusions have been used to treat oxidative stress (50 mg/kg diluted in saline infused over 1 hour).

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

No regulatory information is available. However, because it is short acting and is used primarily for treatment of intoxications, no withdrawal time is suggested. For further information, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Acyclovir**

ay-sye'kloe-veer

**Trade and other names:** Zovirax and generic brands

**Functional classification:** Antiviral

## Pharmacology and Mechanism of Action

Antiviral drug. Acyclovir is a synthetic purine analogue (acyclic nucleoside analogue). It has antiviral activity against herpes virus. The action is related to the affinity for the enzyme thymidine kinase (TK). However, resistance among some virus forms is possible because of changes in TK or in the DNA polymerase. It is used for treatment of various forms of herpes virus infection in humans and also has been used for treatment of viral infections in animals. However, feline herpes virus 1 (FHV1) is resistant to acyclovir and valacyclovir, and studies are lacking on the susceptibility of other herpes viruses. The half-life is 9.6 hours for horses, 2.3 hours for dogs, and 2.6 hours for cats. By comparison, the half-life in humans is 2.5 hours. Unfortunately, it is not absorbed orally in horses (less than 3%), and there are little data to confirm oral absorption in other species. In humans, oral absorption is only 10%. Other forms (e.g., prodrugs and related compounds) are better absorbed in people, but these have been expensive to use in animals. Information on these drugs (penciclovir, valacyclovir, and famciclovir) can be found in other monographs.

## Indications and Clinical Uses

Acyclovir is an antiviral drug. The use in veterinary medicine is limited because the activity against some viruses (e.g., FHV1) is either poor or unknown. In cats, acyclovir had poor absorption and produced toxicity. Acyclovir is able to inhibit replication of equine herpes virus (EHV1) *in vitro*. However, acyclovir oral absorption in horses was poor and inconsistent, and intravenous treatment is needed for treatment of EHV1 infection.

### Precautionary Information

#### Adverse Reactions and Side Effects

The most serious adverse effect in humans is acute renal insufficiency. This may be prevented by slow IV infusion and proper hydration. Phlebitis can occur with IV administration. No adverse effects were identified in limited studies performed in horses, except in one study the IV infusion caused sweating and muscle tremors when administered rapidly (15 min). In cats, significant adverse effects have been observed, which included myelosuppression, hepatotoxicity, and nephrotoxicity.

#### Contraindications and Precautions

Do not use in animals with compromised renal function. Do not use in cats.

#### Drug Interactions

Do not mix with biological solutions (e.g., blood products). Do not mix with fluids that contain bacteriostatic preservatives. Do not use with other nephrotoxic drugs.

## Instructions for Use

To prepare injectable formulation, dilute each vial with 10 or 20 mL of water to make 50 mg/mL. Do not use bacteriostatic water that contains benzyl alcohol or parabens. Further dilute solution to at least 100 mL to a concentration of 7 mg/mL or less.

## Patient Monitoring and Laboratory Tests

Monitor blood urea nitrogen (BUN) and creatinine during use. In horses, doses should be administered to maintain plasma concentrations above 0.3 mcg/mL.

## Formulations

- Acyclovir is available in 400- and 800-mg tablets, 200-mg capsules, 1-g and 500-mg vials for injection (50 mg/mL), and 40-mg/mL oral suspension.

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### Stability and Storage

After reconstitution of solution at 50 mg/mL, it is stable for 12 hours at room temperature. More dilute solutions are stable for 24 hours. If refrigerated, a precipitate will form, which should be redissolved at room temperature before use. Store tablets and capsules in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- Dogs: Systemic doses have not been determined and indications for which it might be effective are not established. Doses have been extrapolated from human use: 3 mg/kg PO five times daily for 10 days, up to 10 mg/kg PO five times daily for 10 days. Alternatively 10-20 mg/kg IV q8h (slow infusion for 1 hour).
- Cats: acyclovir is not effective against feline herpes virus infection and other agents are suggested as alternatives (see famciclovir).

### Large Animal Dosage

#### Horses

- 10 mg/kg q12h IV infused over 1 hour. Even after 20 mg/kg, oral acyclovir is not absorbed in horses well enough for systemic treatment.

### Regulatory Information

Because of mutagenicity, it should not be administered to animals intended for food.

## Afoxolaner

a-fox-olan-er

**Trade and other names:** NexGard

**Functional classification:** Antiparasitic agent (flea and tick insecticide)

### Pharmacology and Mechanism of Action

Afoxolaner belongs to the isoxazolines class of insecticides. A similar agent is fluralaner, another isoxazoline derivative. Afoxolaner has activity against fleas and ticks in dogs. After oral administration by tablet, it is rapidly absorbed and distributed. Fleas and ticks are exposed and killed during their blood meal. Therefore, fleas and ticks first have to bite the host for exposure and effectiveness.

Effects on fleas and ticks occur because isoxazolines, such as afoxolaner, are non-competitive GABA receptor antagonists, but more selective for GABA receptors in insects or ticks, than in animal hosts. As a GABA antagonist, it affects chloride transmission in nerve and muscle cells in fleas and ticks resulting in paralysis and death.

### Indications and Clinical Uses

Alfoxolaner is indicated to kill adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*), and the treatment and control of Black-legged tick (*Ixodes scapularis*), American Dog tick (*Dermacentor variabilis*), Lone Star tick (*Amblyomma americanum*), and Brown dog tick (*Rhipicephalus sanguineus*) infestations in dogs and puppies 8 weeks of age and older, weighing 4 pounds of body weight or greater, for one month.

## Precautionary Information

### Adverse Reactions and Side Effects

Afoxolaner has been safe for use in dogs. Target Animal Safety studies performed in dogs indicate good tolerance at the therapeutic dose. Beagle dogs treated at up to 5 times the therapeutic dose showed no signs of intoxication.

### Drug Interactions

No drug interactions are reported in animals.

### Instructions for Use

Administer oral once per month. Other measures for flea and tick control in the pet's environment also may be used.

## Patient Monitoring and Laboratory Tests

No specific monitoring is needed.

## Formulations

Afoxolaner is available in chewable tablets containing 11.3 mg, 28.3 mg, 68 mg, or 136 mg afoxolaner.

## Stability and Storage

Store at room temperature protected from light in manufacturer's packaging.

## Small Animal Dosage

### Dogs

- 2.5 mg/kg (1.14 mg/lb, PO, once per month during flea and tick season).

### Cats

- No dose for cats has been established.

## Large Animal Dosage

- No large animal doses are available.

## Regulatory Information

- Although risk of harmful residues is low, do not administer to food-producing animals.

## Aglepristone

ag-le'-pri-stone

**Trade and other names:** Alizine or Alzin

**Functional classification:** Hormone, antiprogesterin

## Pharmacology and Mechanism of Action

Aglepristone (RU 46534) is a synthetic steroid antiprogesterin related to mifepristone (RU 38486). It has an affinity for progesterone receptors that is three times that of progesterone, without producing the same effects as progesterone. When administered, it binds to progesterone receptors to produce an antiprogesterin effect and to interrupt and terminate pregnancy.

## Indications and Clinical Uses

Aglepristone has also been used to terminate pregnancy in animals, treat mammary hyperplasia in cats, induce parturition in dogs and cats, and treat pyometra.

## 12 Albendazole

### Precautionary Information

#### Adverse Reactions and Side Effects

After termination of pregnancy in dogs, mucoid discharge may be observed. Other side effects include slight depression, transient anorexia, and mammary gland congestion. Otherwise, there have been no significant adverse effects reported in animals.

#### Contraindications and Precautions

Aglepristone will terminate pregnancy. It should be handled with caution by women. Owners should be cautioned about risks during pregnancy.

#### Drug Interactions

No drug interactions are reported in animals.

### Instructions for Use

For treatment of pyometra, it should be administered on days 1, 2, 7, and 14 by SQ injection.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Aglepristone is not available in the US at this time. In some European countries it is available as a 30-mg/mL injection.

### Stability and Storage

Store at room temperature protected from light.

### Small Animal Dosage

#### Dogs

- Terminate pregnancy: Two doses of 10 mg/kg (0.33 mL/kg) SQ once daily for 2 days.

#### Cats

- Treatment of pyometra: 10 mg/kg SQ, on days 1, 2, 7, and 14.

### Large Animal Dosage

#### Large Animals

- No large animal doses are available.

### Regulatory Information

Do not administer to food-producing animals.

## Albendazole

al-ben'dah-zole

**Trade and other names:** Valbazen

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Benzimidazole antiparasitic drug. Albendazole binds to intracellular beta-tubulin in parasites and prevents the microtubule formation for cell division.

## Indications and Clinical Uses

Albendazole is used to treat a variety of intestinal helminth parasites. It has been used for treating parasitic infections of the respiratory tract, including *Capillaria aero-philia*, *Paragonimus kellicotti*, *Aelurostrongylus abstrusus*, *Filaroides* spp., and *Oslerus osleri*. It is also effective for treatment of *Giardia* in small animals. However, because albendazole has been associated with bone marrow suppression in dogs and cats, other drugs are preferred in small animals for *Giardia*.

### Precautionary Information

#### Adverse Reactions and Side Effects

Leukopenia and thrombocytopenia are possible in dogs and cats. Albendazole has an affinity for rapidly dividing cells and may cause toxicity to bone marrow and intestinal epithelium. High doses have been associated with bone marrow toxicity (*J Am Vet Med Assoc*, 213: 44-46, 1998) in dogs and cats, and it should be used cautiously in small animals. In other species, at approved doses, there is a wide margin of safety. Adverse effects can include anorexia, lethargy, and bone marrow toxicity.

#### Contraindications and Precautions

Adverse effects are more likely when administered for longer than 5 days. Avoid high doses. Pregnancy caution: Do not use during first 45 days of pregnancy.

#### Drug Interactions

No drug interactions are reported in animals.

## Instructions for Use

Used primarily as antihelmintic, but also has demonstrated efficacy for giardiasis.

## Patient Monitoring and Laboratory Tests

Monitor CBC in animals experiencing signs suspicious of adverse effects. If high doses are accidentally administered to small animals, CBC should be examined for evidence of suppression.

## Formulations

- Albendazole is available in a 113.6- and 45.5-mg/mL suspension and 300-mg/mL paste.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been investigated.

## Small Animal Dosage

- Anthelmintic dose: 25-50 mg/kg q12h PO for 3 days.
- Respiratory parasites: 50 mg/kg q24h PO for 10-14 days.
- Giardia: 25 mg/kg q12h PO for 2 days.

### Birds

- 50-100 mg/kg once per day for 2-9 days.

## Large Animal Dosage

### Cattle

- Antiparasitic: Single dose of 10 mg/kg oral paste or 10 mg/kg (suspension) PO.

### Horses

- Dictyocaulus arnfieldi*: 25 mg/kg q12h for 5 days.
- Strongylus vulgaris*: 50 mg/kg q12h for 2 days.



## 14 Albuterol Sulfate

### Sheep and Goats

- Single dose of 7.5 mg/kg oral suspension.

### Regulatory Information

Cattle withdrawal time: 27 days for meat. Do not use in lactating dairy cattle. Sheep withdrawal time: 7 days for meat.

## Albuterol Sulfate

al-byoo'ter-ole sul'fate

**Trade and other names:** Proventil, Ventolin, and Torpex equine inhaler. Also known as Salbutamol outside the US.

**Functional classification:** Bronchodilator, beta-agonist

### Pharmacology and Mechanism of Action

Beta<sub>2</sub>-adrenergic agonist. Albuterol stimulates beta<sub>2</sub>-receptors to relax bronchial smooth muscle. It may also inhibit release of inflammatory mediators, especially from mast cells. This mechanism of action has been beneficial to relax bronchial smooth muscle to relieve bronchospasm and bronchoconstriction.

### Indications and Clinical Uses

Albuterol is indicated in a variety of airway diseases for bronchodilation. Except for equine use, doses are primarily derived from extrapolation of human doses. Efficacy studies for small animal use are not reported. Onset of action is 15-30 minutes, and duration of action may be as long as 8 hours.

Albuterol is used as an inhaler (Torpex) in horses for treatment of airway disease. It provides immediate relief of bronchospasm and bronchoconstriction in horses.

### Precautionary Information

#### Adverse Reactions and Side Effects

Excessive beta-adrenergic stimulation at high doses results in tachycardia and muscle tremors. Arrhythmias are possible with high doses. All beta<sub>2</sub>-agonists will inhibit uterine contractions at the end of gestation in pregnant animals. High doses of beta<sub>2</sub>-agonists can lead to hypokalemia because they stimulate Na<sup>+</sup>-K<sup>+</sup>-ATPase and increase intracellular K<sup>+</sup>, while decreasing serum K<sup>+</sup> and producing hyperglycemia. Treatment consists of KCl supplement at a rate of 0.5 mEq/kg/hr.

#### Contraindications and Precautions

Avoid use in pregnant animals. IM or SQ injections can be painful.

#### Drug Interactions

All beta-agonists will interact with and potentiate other drugs that act on beta-adrenergic receptors.

### Instructions for Use

Administration to horses requires an adaptor to facilitate a metered-dose inhaler. For horses, each valve actuation (puff) of the device delivers 120 micrograms of albuterol sulfate. One dose is three puffs, totaling 360 micrograms. For injection, dilute solution to 0.01 mg/mL (10 mcg/mL) before injection and further dilute to 50/50 with saline or 5% dextrose before injection. When used for bronchoconstriction, it is

helpful for acute exacerbations, used intermittently, with other drugs (e.g., corticosteroids) administered for maintenance.

### Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm in animals with cardiovascular disease. Monitor potassium concentrations for evidence of hypokalemia if high doses are administered. Monitor glucose for evidence of hyperglycemia.

### Formulations

- Albuterol is available in 2- and 4-mg tablets and 2-mg/5-mL syrup. Solutions for inhalation are 0.83 mg/mL and 5 mg/mL. Equine formulation contains 6.7 grams of formulated albuterol sulfate in a pressurized aluminum canister. This formulation delivers 120 micrograms of albuterol sulfate. One dose is three puffs, totaling 360 micrograms.

### Stability and Storage

Store in well-closed containers and protected from light. Aqueous solutions are stable if kept at an acidic pH (2.2-5).

### Small Animal Dosage

#### Dogs and Cats

- 20-50 mcg/kg q6-8h, oral, up to a maximum of 100 mcg/kg q6h.

### Large Animal Dosage

#### Horses

- 120 mcg albuterol per actuation. Administer three actuations, up to a maximum of six, per each dose four times daily.
- Foals: 0.01-0.02 mg/kg, q8-12h, PO.

### Regulatory Information

Do not administer to animals intended for food.

When treating horses, allow 48 hours or longer for urine clearance in performance animals that may be tested.

RCI Classification: 3

## Alendronate

ah-len'droe-nate

**Trade and other names:** Fosamax and generic

**Functional classification:** Antihypercalcemic

### Pharmacology and Mechanism of Action

Bisphosphonate drug. Drugs in this class include pamidronate, risedronate, zoledronate, and etidronate. New drugs approved to treat navicular syndrome in horses are tiludronate (Tildren) and clodronate (OSPHOS). This is a group of drugs characterized by a germinal bisphosphonate bond. They slow the formation and dissolution of hydroxyapatite crystals. Their clinical use is in their ability to inhibit bone resorption. These drugs decrease bone turnover by inhibiting osteoclast activity, retarding bone resorption, and decreasing the rate of osteoporosis. Alendronate is 100-1000 times more potent than older drugs such as etidronate. Unfortunately, alendronate is poorly absorbed orally (3%-7%), and use of oral formulations in animals may not

## 16 Alendronate

be effective. In dogs, half-life in plasma is short (1-2 hours), but there is prolonged uptake of the drug into bone in which the half-life is 300 days.

### Indications and Clinical Uses

Alendronate, like other bisphosphonate drugs, is used in people to treat osteoporosis and treatment of hypercalcemia of malignancy.

In animals, alendronate is used to decrease calcium in conditions that cause hypercalcemia, such as hyperparathyroidism, cancer, and vitamin D toxicosis. It may be helpful for managing neoplastic complications associated with pathologic bone resorption. It also may provide pain relief in patients with pathologic bone disease. Most experimental work performed in dogs has been performed with pamidronate rather than alendronate.

### Precautionary Information

#### Adverse Reactions and Side Effects

No serious adverse effects have been identified; however, use in animals has been uncommon. In people, esophageal injury and erosion are important problems.

When administering to animals, ensure that the entire medication is swallowed and followed with water.

#### Contraindications and Precautions

Do not administer with foods or medications containing calcium. Food will decrease absorption.

#### Drug Interactions

Do not mix with a solution containing calcium (e.g., lactated Ringer's solution).

Do not give with foods containing calcium.

### Instructions for Use

When administering oral medication, ensure that the drug is not trapped in the esophagus in order to avoid injury to esophageal tissue. Food will significantly reduce oral absorption. Wait at least 30 minutes before feeding.

### Patient Monitoring and Laboratory Tests

Monitor serum calcium and phosphorus.

### Formulations

- Alendronate is available in 5-, 10-, 35-, 40-, and 70-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 0.5-1 mg/kg q24h PO.

#### Cats

- Treatment of ionized hypercalcemia: 5-20 mg per cat PO q7d

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Alfaxalone

Al-FAX-ah-lone

**Trade and other names:** Alfaxan (previous name was alphaxalone)

**Functional classification:** Anesthetic agent

### Pharmacology and Mechanism of Action

Alfaxalone is chemically alfaxalone-2-hydroxypropyl-beta-cyclodextrin (HPCD). It is a synthetic neuroactive steroid that interacts with gamma-aminobutyric acid (GABA) receptors in the CNS to produce anesthesia and muscle relaxation. Alfaxalone is related to an older formulation (Saffan) first introduced in 1971, which was alfaxalone plus alfadolone in a combination of neurosteroids. This older formulation was in a castor oil formulation that induced mast cell degranulation and histamine release and produced swollen extremities, anaphylactic reactions, and other signs of histamine release. This new formulation (Alfaxan) overcomes the formulation issue by using a cyclodextrin-solubilizing vehicle. The half-life is short in animals (less than 1 hour), but it exhibits nonlinear pharmacokinetics and may be eliminated slower with high doses.

### Indications and Clinical Uses

Alfaxalone is used as a general anesthetic agent. It can be injected directly into the cephalic vein or delivered via constant-rate infusion. If injected directly, administer over 60 seconds to allow enough time to cross the blood–brain barrier. It has been used safely with other anesthetic agents (e.g., propofol), and in combination with premedications (e.g., opiates, atropine, phenothiazines, benzodiazepines, and nonsteroidal anti-inflammatory drugs [NSAIDs]).

### Precautionary Information

#### Adverse Reactions and Side Effects

As an anesthetic agent, CNS depression, respiratory depression, and some blood pressure decrease are expected after administration. At constant-rate infusion doses  $>0.1$  mg/kg/min it will produce noticeable hypotension and hypoventilation. If injected IM it will cause pain and discomfort. Subcutaneous injection will cause prolonged period of hyper-reactivity and ataxia, but not a good surgical plane of anesthesia. If injected IM, animals will react to sound and recovery can include excitement, incoordination, and hyper-reactivity.

#### Drug Interactions

No drug interactions are reported in animals. It may be used safely with benzodiazepines. However, do not mix with other drugs in the same syringe unless specific compatibility information is available.

### Instructions for Use

For induction of anesthesia, use with appropriate monitoring equipment and ventilatory support. Avoid SQ or IM administration because of pain at injection site. The IM or SQ route is inappropriate for induction and maintenance of anesthesia.

### Patient Monitoring and Laboratory Tests

Monitor character and depth of anesthesia during use. Monitor blood pressure, heart rate, body temperature during anesthesia. Apnea may occur after initial induction. Monitor character and rate of respiration.

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### Formulations

- Alfaxalone is available as 10 mg/mL injectable formulation.

### Stability and Storage

Store at room temperature protected from light. There are no antimicrobial preservatives in the alfaxalone vial. Avoid microbial contamination.

### Small Animal Dosage

#### Dogs

- Induction: 1-5-4.5 mg/kg IV if dogs did not receive a preanesthetic sedative. 0.2-3.5 mg/kg for dogs that received a preanesthetic. Always titrate the dose according to the patient response. Generally, the dose is 1-1.2 mg/kg (up to 2 mg/kg) for each 10 minutes of anesthesia. Deliver dose IV over 60 seconds.
- Constant-rate infusion: 6-7 mg/kg/hour (suitable to use with other anesthetic agents).

#### Cats

- 2.2-9.7 mg/kg IV if cats did not receive a preanesthetic sedative. 1-10.8 mg/kg for cats that received a preanesthetic. Always titrate the dose according to the patient response. Generally, the dose is 1-1.3 mg/kg IV (up to 5 mg/kg) delivered over 60 seconds, followed by sequential doses of 2 mg/kg as needed.
- Loading dose of 1.7 mg/kg IV, followed by constant rate infusion of 7-10 mg/kg/hour IV.

### Large Animal Dosage

#### Large Animals

- No large animal doses are available.

### Regulatory Information

Do not administer to food-producing animals. Alfaxalone is a schedule C-IV controlled substance.

## Allopurinol

al-oh-pyoo'rih-nole

**Trade and other names:** Lopurin, Zyloprim, and Allopur (Europe)

**Functional classification:** Anti-inflammatory

### Pharmacology and Mechanism of Action

Purine analogue. Allopurinol decreases the production of uric acid by inhibiting enzymes responsible for uric acid synthesis. The other use of allopurinol is treating leishmaniasis. In parasites, allopurinol is metabolized to products that disrupt RNA synthesis and interfere with protein synthesis. Allopurinol does not eliminate *Leishmania* or cure the disease, but it may improve cutaneous lesions and induce remission.

### Indications and Clinical Uses

Allopurinol is indicated to decrease formation of uric acid uroliths in at-risk animals. Allopurinol also is used to treat clinical signs associated with leishmaniasis. When used for leishmaniasis, it is administered with pentavalent antimonial compounds such as meglumine antimonite (Glutamine) or sodium stibogluconate (Pentosan).

With chronic treatment, allopurinol will produce progressive remission and improvement in clinical signs associated with leishmaniasis, which include decreasing the damaging effects of *Leishmania* on the animal's kidneys by decreasing proteinuria and preventing deterioration of glomerular filtration rate (GFR).

### Precautionary Information

#### Adverse Reactions and Side Effects

Allopurinol may cause skin reactions (hypersensitivity). In dogs that were treated for leishmaniasis for several months, no adverse effects were reported.

#### Contraindications and Precautions

No contraindications reported for animals.

#### Drug Interactions

Allopurinol may inhibit metabolism of certain drugs. Do not use with azathioprine because it interferes with xanthine oxidase, an important enzyme for metabolizing azathioprine, and will enhance toxicity.

### Instructions for Use

In people, allopurinol is used primarily for treating gout.

In animals, it is used to decrease formation of uric acid uroliths and for treating signs associated with leishmaniasis. No single drug or combination is completely effective for treating leishmaniasis, but allopurinol will improve skin lesions. Allopurinol is usually administered with other drugs for leishmaniasis. For example, it has been administered with either amphotericin B or pentavalent antimonial compounds such as meglumine antimonite (Glutamine) or sodium stibogluconate (Pentosan).

### Patient Monitoring and Laboratory Tests

Dose adjustments for treating leishmaniasis are based on monitoring clinical signs. Allopurinol will not cure the underlying disease, but it will decrease some clinical signs.

### Formulations

- Allopurinol is available in 100- and 300-mg tablets.

### Stability and Storage

Store in well-closed containers at room temperature. Allopurinol is stable for at least 60 days in compounded formulations. Maximum stability in solutions at pH of 3-3.4.

### Small Animal Dosage

#### Dogs

- Urate urolith prevention: 10 mg/kg q8h PO, then reduce to 10 mg/kg q24h PO.
- Leishmaniasis: 10 mg/kg q12h PO for at least 4 months and as long as 6 months. For leishmaniasis, some clinicians have used 15 mg/kg q12h, and then if there is a response, administer 7-10 mg/kg q12-24h PO.

### Large Animal Dosage

#### Horses

- 5 mg/kg PO.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Alprazolam

al-pray-zoe-lam

**Trade and other names:** Xanax and Niravam**Functional classification:** Tranquilizer, CNS depressant

### Pharmacology and Mechanism of Action

Benzodiazepine. Central-acting CNS depressant and anxiolytic (reduces anxiety). Mechanism of action appears to be via potentiation of GABA-receptor-mediated effects in the CNS. A drug that has similar effects is diazepam. In horses the half-life is approximately 16.4 hours.

### Indications and Clinical Uses

Alprazolam is used to treat behavior problems in dogs and cats, particularly those associated with anxiety. Alprazolam has been used in dogs for the short-term treatment of anxiety states, such as noise phobias and thunderstorm phobia. For thunderstorm phobia, it may be more effective if combined with long-term clomipramine treatment. In horses, it has been administered orally. The use in horses is to decrease anxiety, and facilitate a mare-foal bonding, and acceptance of a foal, or orphan foal.

### Precautionary Information

#### Adverse Reactions and Side Effects

Sedation is the most common side effect, but alprazolam may also cause paradoxical excitement in dogs. It has been administered safely to horses without producing noticeable ataxia or sedation at a dose of 0.04 mg/kg. In cats, idiopathic fatal hepatic necrosis has been reported from diazepam, but this has not been reported from alprazolam, probably because of differences in metabolism. Alprazolam is not as extensively metabolized as diazepam. Chronic administration in any species may lead to dependence and a withdrawal syndrome if discontinued.

#### Contraindications and Precautions

No serious contraindications. In rare individuals, benzodiazepines have caused paradoxical excitement.

#### Drug Interactions

Other drugs may decrease hepatic metabolism (e.g., ketoconazole, chloramphenicol, and itraconazole).

### Instructions for Use

Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Duration of effect is only 2-3 hours in many dogs. Therefore, if needed, more frequent administration may be required.

When treating noise phobia (thunderstorm phobia), it is helpful in some dogs to administer 0.02 mg/kg of clomipramine 1 hour before a storm in addition to alprazolam.

The Niravam tablets (see “[Formulations](#)” section) are rapidly dissolving and may be easier to administer to animals that are difficult to medicate. Tablets easily dissolve on the tongue without requiring water and can be cut for accurate dosing.

### Patient Monitoring and Laboratory Tests

Monitor hepatic enzymes in animals with chronic use. Although plasma drug concentrations are usually not measured in animals, 20-40 ng/mL has been associated with therapeutic effects in people.

### Formulations

- Alprazolam is available in 0.25-, 0.5-, 1-, and 2-mg tablets and 1- and 2-mg scored tablets.
- Rapidly dissolving tablets (Niravam) are available in 0.25, 0.5, 1, and 2 mg that can be cut for accurate dosing.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Drug is stable in some compounded formulations for 60 days.

### Small Animal Dosage

#### Dogs

- 0.025-0.1 mg/kg q8h PO. Administration more frequently (q4-6h) has been used in some patients.

#### Cats

- 0.125 mg per cat q12h PO (half of 0.25-mg tablet) or 0.0125-0.025 mg/kg q12h PO, and up to q8h.

### Large Animal Dosage

- Loading dose of 0.1 mg/kg initially, followed by 0.04 mg/kg q12h, PO.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

## Altrenogest

al-tren'-oh-jest

**Trade and other names:** Regu-Mate, Matrix

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Altrenogest is an active synthetic progestin hormone. As a progesterone agonist, it is primarily used to suppress estrus in animals. Suppression of estrus allows for a predictable occurrence of estrous activity after the drug is discontinued. Therefore it is used to induce a normal cycle of estrous activity to facilitate scheduled breeding. When treatment is initiated, 95% of the mares will have an estrous cycle suppressed in 3 days.

### Indications and Clinical Uses

Altrenogest is indicated to suppress estrus in animals to facilitate induction of normal estrous cycle activity. It is used in mares to facilitate scheduled breeding activity. It is also used to suppress estrous behavior in performance horses. When treatment is discontinued, mares exhibiting regular estrous cycles return to estrus within 4 to 5 days following treatment and continue to cycle normally.

In swine, altrenogest is used for synchronization of estrus in sexually mature gilts that have had at least one estrous cycle. Do not use in gilts having a previous or current history of uterine inflammation (i.e., acute, subacute, or chronic endometritis).



### Precautionary Information

#### Contraindications and Precautions

Do not administer to pregnant animals. Humans handling altrenogest, particularly women, should wear gloves and avoid contact because altrenogest can be absorbed in humans through intact skin. Altrenogest should not be used in mares or in gilts with a previous history of uterine problems (metritis).

### Instructions for Use

Administer altrenogest 1 dose daily for 15 days, orally on grain or directly on the horse's tongue. In pigs, administer as a top dressing or with feed.

### Patient Monitoring and Laboratory Tests

Monitor for signs of estrous activity. Monitor CBC in cases of overdose.

### Formulations

- Altrenogest is available in an oil solution of 0.22% (2.2 mg/mL).

### Stability and Storage

Store in well-closed containers at room temperature.

### Small Animal Dosage

- No dose available.

### Large Animal Dosage

#### Horses

- 0.044 mg/kg (or 1 mL per 110 pounds) orally once per day for 15 days.

#### Swine

- Administer 6.8 mL (15 mg altrenogest) per gilt once daily for 14 consecutive days by top-dressing on a portion of each gilt's daily feed.

### Regulatory Information

Do not use in horses intended for food. In pigs, gilts must not be slaughtered for human consumption for 21 days after the last treatment. Do not administer to other food-producing animals.

## Aluminum Hydroxide and Aluminum Carbonate

ah-loo'mih-num hye-droks'ide, ah-loo'mih-num kar'boe-nate

**Trade and other names:** Aluminum hydroxide gel (Amphojel) and aluminum carbonate gel (Basaljel)

**Functional classification:** Antacid

### Pharmacology and Mechanism of Action

Aluminum is an antacid and phosphate binder in intestine. It is used in both the aluminum hydroxide and aluminum carbonate formulations.

### Indications and Clinical Uses

A common use of aluminum hydroxide is for its antacid properties to treat or manage gastrointestinal ulcers. Also, it is used as a phosphate binder. It is indicated in animals with hyperphosphatemia associated with chronic renal failure, often in combination with phosphorus-restricted diets. Because of the decreased availability of products

containing aluminum, other drugs are used to decrease hyperphosphatemia in patients, such as calcium carbonate and calcium citrate. A new oral phosphate binder is available in some countries for cats. This product (Lenziaren) consists of a complex of iron oxide/hydroxide and is administered orally to cats.

### Precautionary Information

#### Adverse Reactions and Side Effects

These aluminum-containing compounds are generally safe. However, there has been some concern expressed that these drugs may increase the systemic levels of aluminum, which may lead to some forms of aluminum toxicoses. The evidence for this as a clinical problem in veterinary medicine is lacking.

#### Contraindications and Precautions

Aluminum decreases oral absorption of some drugs (e.g., fluoroquinolones, tetracyclines). If fluoroquinolone antimicrobials are used concurrently, separation of oral doses should be considered.

#### Drug Interactions

Aluminum will bind and chelate some drugs and prevent the GI absorption. Drugs bound to aluminum include tetracyclines and quinolone antibiotics.

### Instructions for Use

Antacid doses are designed to neutralize stomach acid, but duration of acid suppression is short. Although aluminum hydroxide is often used to prevent hyperphosphatemia, this drug may not be available in some pharmacies. A substitute for this indication is calcium citrate or calcium carbonate. An oral product is also available for cats to administer as a phosphate binder (Lenziaren) which is a complex of iron oxide/hydroxide.

### Patient Monitoring and Laboratory Tests

Phosphate plasma levels should be monitored to determine success of therapy.

### Formulations

- Aluminum hydroxide gel is available in a 64-mg/mL oral suspension and 600-mg tablet.
- Aluminum carbonate gel is available in capsules (equivalent to 500 mg aluminum hydroxide).
- Note: Products containing aluminum may no longer be available from many sources, and other products may be used, such as Lenziaren, which is a complex of iron oxide/hydroxide for cats.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- Aluminum hydroxide gel: 10-30 mg/kg q8h PO (with meals).
- Aluminum carbonate gel: 10-30 mg/kg q8h PO (with meals).

#### Cats

- Aluminum hydroxide gel: 10-30 mg/kg q8h PO (with meals).
- Aluminum carbonate gel: 10-30 mg/kg q8h PO (with meals).

### Large Animal Dosage

#### Horses

- Antacid: 60 mg/kg q8h PO.

## Regulatory Information

No regulatory information is available. Residues from administration to food-producing animals ordinarily are not a concern. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Amantadine

ah-man'tah-deen

**Trade and other names:** Symmetrel and generic brands

**Functional classification:** Antiviral

## Pharmacology and Mechanism of Action

Amantadine is an antiviral drug. The action against viruses is not entirely known. For treating other conditions in people (Parkinson's disease), its effects are attributed to an increase in dopamine in the CNS. However it also is an N-methyl-D-aspartate (NMDA) receptor antagonist. As an NMDA antagonist, it will decrease tolerance to other analgesic drugs (e.g., opiates), but it probably does not possess many analgesic properties when used alone. There is only limited pharmacokinetic data available for animals. The oral formulation is completely absorbed from oral administration in people and animals and crosses the blood-brain barrier. In cats the half-life was approximately 6 hours; in dogs the half-life is approximately 5 hours.

## Indications and Clinical Uses

Amantadine is an antiviral drug used to treat influenza infections in people. It also is used in people to treat Parkinson disease and extrapyramidal reactions, especially those that are drug induced. It also has been used to manage muscular weakness in humans with multiple sclerosis. However, its use in veterinary medicine has primarily been for treating pain in dogs and cats. It is used for treating pain when other drugs have been ineffective or when it is desirable to use in combination with multiple drugs in multimodal therapy analgesic protocols.

## Precautionary Information

### Adverse Reactions and Side Effects

Toxicity has not been seen in dogs and cats until doses are exceeded by at least two times. Rarely, the side effects of anxiety states and dry mouth have been observed. Dizziness, confusion, and other CNS disturbances have been reported in people.

### Contraindications and Precautions

Pregnancy caution: Amantadine is embryotoxic and teratogenic at high doses in laboratory animals. Avoid its use in pregnancy.

### Drug Interactions

Do not use with other drugs that increase dopamine concentrations (e.g., selegiline). If used with other CNS stimulants, it may enhance the effects.

## Instructions for Use

Amantadine for treatment of pain may not be effective when used alone. Administer with another analgesic agent (e.g., NSAID) for best results. In post-surgical patients it has been used for up to 21 days without adverse effects. Antiviral effects have not

been adequately explored in animals. In people, antiviral dose is 1.5-3 mg/kg once or twice a day.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Amantadine is available in 100-mg capsules, 100-mg tablets, and 10-mg/mL syrup.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- For pain treatment, 3-5 mg/kg q12h, PO.

#### Cats

- 3 mg/kg q24h PO for treatment of pain, up to a dose of 5 mg/kg in some cases.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

This drug should not be administered to food-producing animals, and no regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Amikacin

am-ih-kay'sin

**Trade and other names:** Amiglyde-V (veterinary preparation), Amikin (human preparation), and generic brands

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Aminoglycoside antibiotic. Action is to inhibit bacteria protein synthesis via binding to 30S ribosome. Amikacin is bactericidal with a broad spectrum of activity except against streptococci and anaerobic bacteria. Amikacin may have activity against many bacteria, especially gram-negative bacilli, that are resistant to other drugs. Amikacin may be more active than gentamicin against many gram-negative bacteria, especially enteric species. In most animals, the half-life is short (1-2 hours), and volume of distribution reflects extracellular body water (e.g., 200-250 mL/kg). Amikacin is not absorbed from oral administration.

### Indications and Clinical Uses

Amikacin is indicated in bacterial infections, especially for treatment of serious infections caused by gram-negative bacteria. When resistance to gentamicin is anticipated, amikacin is often used in its place. In horses, amikacin also is used for local administration as an intrauterine lavage to treat metritis and other infections of the genital tract caused by gram-negative bacteria. In horses, amikacin also is used for regional limb perfusion.

**Precautionary Information****Adverse Reactions and Side Effects**

Nephrotoxicity is the most dose-limiting toxicity. Ensure that patients have adequate fluid and electrolyte balance during therapy. Ototoxicity and vestibulotoxicity also are possible.

**Contraindications and Precautions**

Do not use in animals with renal insufficiency or renal failure. Do not use in dehydrated animals.

**Drug Interactions**

Do not mix in vial or syringe with other antibiotics. Amikacin is incompatible with other drugs and compounds when mixed in the same vial or syringe. This effect is particularly important when mixing with other antibiotics. When used with anesthetic agents, neuromuscular blockade is possible.

**Instructions for Use**

Once-daily doses are designed to maximize peak-to-minimum inhibitory concentration (MIC) ratio. Consider therapeutic drug monitoring to decrease risk of renal toxicity. Activity against some bacteria (e.g., *Pseudomonas*) is enhanced when combined with a beta-lactam antibiotic. Nephrotoxicity is increased with persistently high trough concentrations.

**Patient Monitoring and Laboratory Tests**

Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) MIC breakpoint is  $\leq 4$  mcg/mL for dogs and horses and  $\leq 2$  mcg/mL for foals. The canine breakpoint also can be applied to bacterial isolates from cats. Monitor BUN, serum creatinine, and urine for evidence of renal toxicity. Plasma or serum drug concentrations can be monitored to measure for problems with systemic clearance. When monitoring trough levels in patients during once-daily administration, the trough levels should fall below the limit of detection. Alternatively, the half-life and clearance can be measured from samples taken at 1 hour and 2 to 4 hours postdosing. Clearance in most animals should be above 1.0 mL/kg/min and half-life should be  $< 2$  hours.

**Formulations**

- Amikacin is available in 50- or 250-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Amikacin will be unstable if mixed with other drugs.

**Small Animal Dosage****Dogs**

- 15-30 mg/kg q24h IV, IM, or SQ.

**Cats**

- 10-14 mg/kg q24h IV, IM, or SQ.

**Large Animal Dosage****Horses**

- Adult: 4.4-6.6 mg/kg q12h IM or IV or 10 mg/kg q24h IV or IM.
- Foal: 20-25 mg/kg q24h IV or IM or 6.6 mg/kg q8h IV or IM.
- Intrauterine use: Administer 2 g (8 mL) diluted in 200-mL sterile saline solution in uterus once per day for 3 days.
- Regional limb perfusion: Doses have ranged from 125 mg to 500 mg per limb, diluted in 60 mL saline.

**Cattle**

- Adult: 10 mg/kg q24h IM, IV, or SQ.
- Calf (<2 weeks of age): 20 mg/kg q24h IV or IM.

**Regulatory Information**

Withdrawal times have not been established for extralabel use in animals used for food. Long persistence of drug in tissues (renal) is expected after administration. Amikacin, like other aminoglycoside antibiotics, should not be administered to animals that produce food because of a risk of residue problems. If extralabel doses have been administered, the meat withdrawal time may be as long as 18 months. Contact FARAD at 1-888-USFARAD (1-888-873-2723) for specific withdrawal time information.

**Amino Acid Solution**

**Trade and other names:** Travasol

**Functional classification:** Amino acid solution

**Pharmacology and Mechanism of Action**

Amino acid solutions are intended to provide amino acid supplement to animals with amino acid deficiency or with liver disorders. This particular solution contains leucine, phenylalanine, lysine, methionine, isoleucine, valine, histidine, threonine, tryptophan, alanine, glycine arginine, proline, tyrosine, and serine.

**Indications and Clinical Uses**

In animals, amino acid solutions are infused to provide supplement, particularly for treatment of liver disease.

**Precautionary Information****Adverse Reactions and Side Effects**

A hyperosmolar state can be induced if the infusion is too aggressive. If neurologic signs appear, the infusion should be stopped. In patients with liver disease or renal failure, hepatic encephalopathy or increases in BUN are possible.

**Instructions for Use**

10% solution may be diluted in 5% dextrose solution for peripheral vein administration. Otherwise, it should be administered via a central vein.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- 10%, 5.5% and 8.5% solutions.

**Stability and Storage**

Store at room temperature protected from light.

**Small Animal Dosage****Dogs**

- 25 mL of a 10% solution (diluted appropriately) infused IV via a central vein. Administer infusion over 6-8 hours and repeat at 7- to 10-day intervals. Solutions without electrolytes are preferred for treating hepatocutaneous syndrome.

## 28 Aminopentamide

### Large Animal Dosage

#### Large Animals

- No dose reported.

### Regulatory Information

There is no withdrawal time necessary for food animals.

## Aminopentamide

ah-mee-noe-pent'ah-mide

**Trade and other names:** Centrine

**Functional classification:** Anticholinergic

### Pharmacology and Mechanism of Action

Antidiarrheal drug. Anticholinergic (blocks acetylcholine at parasympathetic synapse). Like other anticholinergic drugs in this class, aminopentamide blocks muscarinic receptors. As a result of blockade, effects of acetylcholine are blocked to inhibit gastrointestinal secretions and smooth muscle motility. Glandular, respiratory, and other physiologic functions also can be affected. Aminopentamide is an older drug that is not often used as a treatment of diarrhea or gastrointestinal diseases today.

### Indications and Clinical Uses

Aminopentamide has been used to decrease gastrointestinal motility and decrease gastrointestinal secretions in animals. It also has been used to treat diarrhea, but long-term use for this purpose is not recommended.

### Instructions for Use

Dosing guidelines based on manufacturer's recommendation.

### Patient Monitoring and Laboratory Tests

Monitor for problems caused by intestinal stasis because of anticholinergic effect.

### Formulations

- Aminopentamide is available in 0.2-mg tablets and 0.5-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 0.01-0.03 mg/kg q8-12h IM, SQ, or PO.

#### Cats

- 0.1 mg/cat q8-12h IM, SQ, or PO.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Aminophylline

am-in-off'ih-lin

**Trade and other names:** Generic brands

**Functional classification:** Bronchodilator

### Pharmacology and Mechanism of Action

Bronchodilator. Aminophylline is a salt of theophylline, formulated to enhance oral absorption without gastric side effects. It is converted to theophylline after ingestion. The mechanism of action and other properties are the same as theophylline. Consult the theophylline monograph for more details. Theophylline's action is to inhibit phosphodiesterase (PDE) and increase cyclic adenosine monophosphate (cAMP). Other anti-inflammatory mechanisms also may play a role in its clinical effects.

### Indications and Clinical Uses

Aminophylline is indicated for control of reversible airway constriction, to prevent bronchoconstriction, and as an adjunct with other respiratory disease treatment. The uses are similar to the indications for theophylline because it is a salt form of theophylline. It is used for inflammatory airway disease in cats (feline asthma), dogs, and horses. In dogs, the uses include collapsing trachea, bronchitis, and other airway diseases. It has not been effective for respiratory diseases in cattle. The oral forms have mostly been discontinued and only the injection forms remain. For oral administration, theophylline should be used.

### Precautionary Information

#### Adverse Reactions and Side Effects

Aminophylline causes excitement and possible cardiac side effects with high concentrations. Cardiac adverse effects include tachycardia and arrhythmias. Gastrointestinal adverse effects include nausea, vomiting, and diarrhea. Central nervous system adverse effects include excitement, tremors, and seizures.

#### Contraindications and Precautions

Although adverse effects appear more common in people than small animals, use cautiously in animals with cardiac arrhythmias. Use cautiously in animals prone to seizures. Horses may become excited from IV administration.

#### Drug Interactions

Use cautiously with other phosphodiesterase inhibitors such as sildenafil (Viagra) and pimobendan. Many drugs will inhibit the metabolism of theophylline and potentially increase concentrations (e.g., cimetidine, erythromycin, fluoroquinolones, and propranolol). Some drugs will decrease concentrations by increasing metabolism (e.g., phenobarbital and rifampin).

### Instructions for Use

Therapeutic drug monitoring of theophylline is recommended for accurate dosing during chronic therapy. When dosing with salts or other formulations of theophylline, adjust dose for the amount of the parent drug. The oral forms have been discontinued and the dosing listed applies to injection formulation. For oral administration, use theophylline.



## 30 Amiodarone Hydrochloride

### Patient Monitoring and Laboratory Tests

Plasma concentrations of theophylline should be monitored in patients receiving therapy with aminophylline. Targeted plasma concentrations range from 10-20 mcg/mL, but clinical effects may occur as low as 5 mcg/mL.

### Formulations

- Aminophylline is available in 25-mg/mL injection. A dose of 25 mg/mL of anhydrous aminophylline is equivalent to 19.7 mg of anhydrous theophylline per mL. Oral forms have been discontinued; for oral administration use theophylline instead.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Compounded oral formulations have been stable for 60 days.

### Small Animal Dosage

#### Dogs

- 10 mg/kg q8h IM, or IV.

#### Cats

- 6.6 mg/kg q12h, IM or IV.

### Large Animal Dosage

#### Horses

- Treatment of recurrent airway obstructions: 12 mg/kg initial dose, followed by 5 mg/kg q12h. Aminophylline administered IV to horses has caused transient excitement and restlessness. Give IV administration slowly.

#### Cattle

- 10 mg/kg q8h IV or 23 mg/kg PO, administered once as a single dose.

### Regulatory Information

Cattle: No withdrawal times have been established for food animals.

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Amiodarone Hydrochloride

ah-mee-oe'dah-rone

**Trade and other names:** Cordarone

**Functional classification:** Antiarrhythmic

### Pharmacology and Mechanism of Action

Antiarrhythmic drug, Class III. Antiarrhythmic effects are primarily caused by blocking the outward potassium channel in cardiac tissues. Amiodarone prolongs the action potential, delays myocardial repolarization, and delays the refractory period in cardiac tissues. It also may have some alpha-adrenergic receptor, beta-adrenergic receptor, and calcium-channel blocking properties. Half-life is several days in duration, and in some animals the half-life may be as long as 100 days with chronic therapy. In horses the terminal half-life was 38-84 hours. The intravenous formulation of amiodarone uses Polysorbate 80 to enhance solubility, which may be responsible for some of the adverse reactions. There is a new noniodinated derivative, dronedarone (Multaq), that is less lipophilic, has a shorter half-life, and may be safer, but there has been no use reported in animals.

## Indications and Clinical Uses

Amiodarone is used to treat refractory ventricular arrhythmias. It is reserved for treating life-threatening arrhythmias that have been refractory to other treatments. It has been used as a last resort for recurrent hemodynamically unstable ventricular tachycardia.

In horses, IV amiodarone has been used to treat atrial fibrillation.

## Precautionary Information

### Adverse Reactions and Side Effects

The most common effect in dogs is decreased appetite. Prolonged Q-T interval is a concern. Other adverse effects include bradycardia, congestive heart failure (CHF), hypotension, atrioventricular (AV) block, thyroid dysfunction (decreased  $T_3$  and  $T_4$ ), pulmonary fibrosis, neutropenia, and anemia. Hepatopathy is a serious concern and has been reported in dogs. Doberman dogs were particularly affected by amiodarone when treated for arrhythmias; there was a high incidence of adverse effects that included anorexia, lethargy, hepatic toxicity, and vomiting. In one study, doses up to 12.5 mg/kg IV produced no acute cardiovascular reactions; however, with acute IV administration, severe cardiac reactions, hypotension, vasodilation, pruritus, and edema (including swollen extremities) are possible. Adverse effects caused by IV treatment may be caused by the drug vehicle included to enhance solubility, Polysorbate 80, which is known to elicit allergic-type adverse events caused by histamine release. Pretreatment with antihistamines may help to decrease adverse events caused by IV treatment.

No adverse clinical signs were observed in horses after single-administration IV, but for treating atrial fibrillation, mild signs of shifting weight and hind limb weakness were reported.

### Contraindications and Precautions

Severe reactions, including hepatopathy and cardiac arrhythmias, have been seen in dogs. Use only when arrhythmia has been refractory to other treatments or when dogs are at risk for sudden death.

### Drug Interactions

Use amiodarone with beta blockers, calcium-channel blockers, and digoxin cautiously because it may slow conduction. Do not mix IV solution with mixtures containing bicarbonate.

## Instructions for Use

Typically, loading doses are administered, followed by maintenance dose. Oral dosing in dogs has used 10-15 mg/kg q12h for 1 week, then 5-7.5 mg/kg q12h for 2 weeks, followed by maintenance dose of 7.5 mg/kg q24h. If IV therapy is used, doses should be given slowly; initial infusion rate should not exceed 30 mg per minute. Prior to IV treatment, administer antihistamines to prevent allergic-type reactions.

## Patient Monitoring and Laboratory Tests

Because of a concern for adverse effects caused by amiodarone in dogs, therapy should be monitored carefully. It is highly recommended to monitor CBC for anemia and neutropenia and monitor hepatic indices with biochemical profile during treatment. Monitor electrocardiogram (ECG) during treatment, as prolonged Q-T interval may occur. Monitor thyroid function during treatment. Drug monitoring may be available from some laboratories. Therapeutic range of amiodarone in plasma is 1-2.5 mcg/mL.

## Formulations

Amiodarone is available in 100- and 200-mg tablets and 50-mg/mL injection, and a 1.5 mg/mL and a 1.8 mg/mL injectable under the name Nexterone. A new formulation (PM101) uses a different vehicle to enhance solubility rather than Polysorbate 80. This vehicle, beta-cyclodextrin (Captisol), forms a hydrophilic central core and is less likely to elicit an allergic-type reaction.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- Ventricular arrhythmias: 10-15 mg/kg q12h PO for 1 week, then 5-7.5 mg/kg q12h for 2 weeks, followed by maintenance dose of 7.5 mg/kg q24h.
- Refractory arrhythmias: 25 mg/kg q12h PO for 4 days, followed by 25 mg/kg q24h PO.
- Atrial fibrillation: 15 mg/kg loading dose for 5 days, followed by 10 mg/kg per day, PO, thereafter.
- Boxer or Doberman: 200 mg per dog q12h for 1 week, PO, followed by 200 mg once daily thereafter. Doses as high as two times these rates have been administered, but with a higher risk of toxicity.
- Injection: 5 mg/kg, slowly IV over 10 minutes. Use cautiously because of risk of adverse effects.

### Cats

- No dose has been reported for cats.

## Large Animal Dosage

### Horses

- Treatment of atrial fibrillation: 5 mg/kg/hr for 1 hour, followed by 0.83 mg/kg/hr for 23 hours IV. Oral absorption was low and inconsistent and has not been recommended.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Amitraz

am'ih-traz

**Trade and other names:** Mitaban

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Antiparasitic drug for ectoparasites. Amitraz inhibits monoamine oxidase (MAO) in mites. Mammals are resistant to this inhibition. However, administration of amitraz can interact with other MAO inhibitors (MAOIs).

## Indications and Clinical Uses

Amitraz is indicated for the topical treatment of mites, including Demodex. It is applied topically as a dip or sponge-on. It should not be administered systemically. The approved dose is effective in many animals; however, in more resistant cases of

Demodex, higher doses have been applied. As the dose increases, the risk of adverse effects also increases.

### Precautionary Information

#### Adverse Reactions and Side Effects

Amitraz causes sedation in dogs caused by the agonist activity on  $\alpha_2$ -adrenergic receptors, which may be reversed by yohimbine or atipamezole. When high doses are used, other side effects reported include pruritus, polyuria/polydipsia, bradycardia, hypotension, heart block, hypothermia, hyperglycemia, and (rarely) seizures.

#### Contraindications and Precautions

Adverse effects are more common when high doses are administered.

#### Drug Interactions

Do not administer with MAOIs, such as selegiline (Deprenyl, Anipryl). Do not administer with other  $\alpha_2$ -agonists.

### Instructions for Use

Manufacturer's dose should be used initially, but for refractory cases, this dose has been exceeded to produce increased efficacy.

### Patient Monitoring and Laboratory Tests

Monitor by performing periodic skin scrapings and examining for presence of mites.

### Formulations

- Amitraz is available in 10.6-mL concentrated dip (19.9%).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 10.6 mL/7.5 L water (0.025% solution). Apply three to six topical treatments every 14 days. For refractory cases, this dose has been exceeded to improve efficacy. Doses that have been used include 0.025%, 0.05%, and 0.1% concentration applied once or twice per week. For refractory cases, a dose of 0.125% has been used by applying to only one half of the dog's body one day, then to the other half of the body the following day. This alternating schedule has been repeated every day for 4 weeks and up to 5 months to achieve cures, but should be considered only in extreme cases.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Amitriptyline Hydrochloride

am-ih-trip'tih-leen hye-droe-klor'ide

**Trade and other names:** Elavil and generic brands

**Functional classification:** Behavior modification, tricyclic antidepressant (TCA)

### Pharmacology and Mechanism of Action

TCA drug. Amitriptyline, like other TCAs, acts via inhibition of the uptake of serotonin and other transmitters at presynaptic nerve terminals. The action in cats for treating cystitis is unknown, but may be either through reducing anxiety, behavior modification, or anticholinergic effects.

### Indications and Clinical Uses

Like other TCAs, amitriptyline is used in animals to treat a variety of behavioral disorders (e.g., anxiety). However, there are few studies documenting efficacy in animals. For treatment of some disorders, such as obsessive compulsive disorder (1 mg/kg q12h up to 2 mg/kg), it was not as effective in animals as clomipramine. For treatment of aggressive behavior in dogs (2 mg/kg q12h), there was no difference between amitriptyline and placebo.

Amitriptyline has been used in cats for chronic idiopathic cystitis. However, when used for short-term treatment of idiopathic cystitis (10 mg per cat, q24h) it was not effective. In another study, at 5 mg/cat per day for 7 days (0.55-1.2 mg/kg), there was no difference on recovery from hematuria and pollakiuria between amitriptyline and placebo, leading to a conclusion that short-term treatment is not helpful.

### Precautionary Information

#### Adverse Reactions and Side Effects

Amitriptyline has a bitter taste and is difficult to administer orally. Multiple side effects are associated with TCAs, such as antimuscarinic effects (dry mouth and rapid heart rate) and antihistamine effects (sedation). High doses can produce life-threatening cardiotoxicity. In cats, reduced grooming, weight gain, and sedation are possible.

#### Contraindications and Precautions

Use cautiously in patients with heart disease.

#### Drug Interactions

Do not use with other behavior modification drugs, such as serotonin reuptake inhibitors. Do not use with MAOIs.

### Instructions for Use

Doses are primarily based on empiricism. There are no controlled efficacy trials available for animals. There is evidence for success treating idiopathic cystitis in cats (*J Am Vet Med Assoc*, 213: 1282-1286, 1998). Amitriptyline was not effective for treatment of aggressive behavior in dogs, compared to behavior modification alone (*J Am Anim Hosp Assoc*, 37: 325-330, 2001). Amitriptyline applied transdermally is not systemically absorbed in cats.

### Patient Monitoring and Laboratory Tests

Monitor patient's cardiovascular status during therapy, such as heart rate and rhythm. Like other TCAs, amitriptyline may decrease total T<sub>4</sub> and free-T<sub>4</sub> concentrations in dogs.

### Formulations

- Amitriptyline is available in 10-, 25-, 50-, 75-, 100-, and 150-mg tablets. The injectable formulation is no longer marketed in the US.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 1-2 mg/kg q12-24h PO.

### Cats

- 2-4 mg per cat/day PO (0.5-1.0 mg/kg PO per day). The dose for cats may be divided into 12-hour intervals.
- Idiopathic cystitis: 2 mg/kg/day PO, or a range of 2.5-7.5 mg/cat/day.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

## Amlodipine Besylate

am-loe'dih-peen bess'ih-late

**Trade and other names:** Norvasc

**Functional classification:** Calcium-channel blocker

## Pharmacology and Mechanism of Action

Calcium-channel blocking drug. Amlodipine is a calcium-channel blocker of the dihydropyridine class. It decreases calcium influx in cardiac and vascular smooth muscle. Its greatest effect is on vascular smooth muscle, acting as a vasodilator.

## Indications and Clinical Uses

In cats and dogs it is used to treat systemic hypertension (high blood pressure). Hypertension in cats has been defined as systolic blood pressure > 190 mm Hg and diastolic pressure > 120 mm Hg. Amlodipine is considered the drug of choice by many clinicians for treating hypertension in cats. By comparison, angiotensin-converting enzyme (ACE) inhibitors are less effective in cats and they respond better to amlodipine than to ACE-inhibitors. Amlodipine may improve survival in cats with hypertensive kidney disease. In cats, addition of a beta blocker to slow heart rate may also be beneficial.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects can include hypotension and bradycardia. In dogs, gingival hyperplasia has been observed, which may be caused by an up-regulation of circulating androgens or inhibition of transglutaminase. It usually resolves after discontinuation of the medication.

### Contraindications and Precautions

Use cautiously in animals with poor cardiac reserve and that are prone to hypotension. Do not use in dehydrated animals.

**Drug Interactions**

Use cautiously with other vasodilators. Drug interactions are possible from concurrent use with phenylpropanolamine, theophylline, and beta-agonists.

**Instructions for Use**

In cats, efficacy has been established at 0.625 mg/cat once daily. If cats are large size (>4.5 kg) or refractory, increase dose to 1.25 mg/cat q24h PO. In some cats, addition of a beta blocker to slow heart rate may be indicated. The goal of treatment is to decrease systolic pressure to less than 150/90 (systolic/diastolic).

**Patient Monitoring and Laboratory Tests**

Monitor patient's blood pressure if possible. Cats with high pressures of systolic 160-190 mm Hg and diastolic 100-120 mm Hg should be considered at risk of clinical effects from hypertension.

**Formulations**

- Amlodipine is available in 2.5-, 5-, and 10-mg tablets. (Tablets are difficult to split for small animals.)

**Stability and Storage**

Amlodipine is an unstable drug, and potency and stability are not assured if the original formulation is disrupted or compounded. Store in a tightly sealed container and protect from light.

**Small Animal Dosage****Dogs**

- 2.5 mg/dog or 0.1-0.5 mg/kg q24h PO. The higher dose of 0.5 mg/kg may be needed in refractory cases to reduce blood pressure.

**Cats**

- 0.625 mg/cat initially q24h PO and increase if needed to 1.25 mg/cat. Average recommended dose for most cats is 0.18 mg/kg; once daily for hypertension.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

**Ammonium Chloride**

ah-moe'nee-um klor'ide

**Trade and other names:** Generic brands

**Functional classification:** Acidifier

**Pharmacology and Mechanism of Action**

Urine acidifier. After oral administration, ammonium chloride induces acidic urine.

## Indications and Clinical Uses

Compounds containing ammonium are administered to patients to acidify the urine, primarily to manage cystic calculi or chronic urinary tract infections (UTIs).

### Precautionary Information

#### Adverse Reactions and Side Effects

Ammonium chloride has a bitter taste when added to food. It may cause acidemia in some patients if administered at high doses.

#### Contraindications and Precautions

Do not use in patients with systemic acidemia. Use cautiously in patients with renal disease. It may be unpalatable when added to some animals' food.

#### Drug Interactions

No drug interactions are reported in animals.

## Instructions for Use

Doses are designed to maximize urine acidifying effect.

## Patient Monitoring and Laboratory Tests

Monitor patient's acid/base status.

## Formulations

- Ammonium is available as crystals.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 100 mg/kg q12h PO.

### Cats

- 800 mg/cat, or 20 mg/kg (approximately one-third to one-quarter teaspoon) mixed with food daily.

## Large Animal Dosage

### Horses

- Acidifier: 100-250 mg/kg q24h PO.

## Regulatory Information

No regulatory information is available. It is not expected to pose a residue risk, and no withdrawal is recommended for food animals.

## Amoxicillin

ah-moks-ih-sill'in

**Trade and other names:** Amoxicillin: Amoxi-Tabs, Amoxi-Drops, Amoxi-Inject, Robamox-V, Biomox, and other brands. Amoxil, Trimox, Wymox, Polymox (human preparation), and amoxicillin trihydrate

**Functional classification:** Antibacterial



## Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Amoxicillin inhibits bacterial cell wall synthesis. Amoxicillin generally has a narrow spectrum of activity that includes streptococci, non-beta-lactamase-producing staphylococci, and other gram-positive cocci and bacilli. Many *Staphylococcus* strains are resistant due to beta-lactamase production. Most enteric gram-negative bacilli of the Enterobacteriaceae are resistant. Susceptible gram-negative bacteria include some species of *Proteus*, *Pasteurella multocida*, and *Histophilus*. Resistance among gram-negative bacteria is common.

In dogs, the peak concentration, half-life, volume of distribution (VD/F), and clearance (CL/F) are 11 mcg/mL, 1.3 hours, 0.72 L/kg, and 6.5 mL/kg/min, respectively. In cats, these values are 12 mcg/mL, 1.4 hours, 1.05 L/kg, and 7.8 mL/kg/min, respectively. Amoxicillin oral absorption in small animals is higher than ampicillin (two times higher in some animals). Amoxicillin oral absorption in adult horses is <10% and is not recommended. In pigs oral absorption is approximately 40% with a half-life after oral administration of 45 minutes.

## Indications and Clinical Uses

Amoxicillin is used for a variety of infections in all species, including UTI, soft tissue infections, and pneumonia. It is generally more effective for infections caused by gram-positive bacteria. Because of a short half-life, frequent administration is needed for treating gram-negative infections. In addition, break point for susceptibility is higher for gram-negative versus gram-positive organisms. Oral absorption in horses is <10%, and it is not suitable for treatment of adult horses. However, oral absorption in foals is 36%-43%. Oral absorption in small animals is 50%-60%.

### Precautionary Information

#### Adverse Reactions and Side Effects

Amoxicillin is usually well tolerated. Allergic reactions are possible. Diarrhea and vomiting are common with oral doses. Oral administration to horses or cattle can cause diarrhea and/or enteritis.

#### Contraindications and Precautions

Use cautiously in animals allergic to penicillinlike drugs.

#### Drug Interactions

Do not mix with other drugs in compounded formulations.

## Instructions for Use

Dose recommendations vary depending on the susceptibility of bacteria and location of infection. Generally, more frequent or higher doses are needed for gram-negative infections.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: For testing for susceptibility, the CLSI recommends using ampicillin to test for amoxicillin susceptibility. The CLSI break point for sensitive organisms is  $\leq 0.25$  mcg/mL for staphylococci, streptococci, and gram-negative bacilli. For canine urinary tract pathogens, use a break point of  $\leq 8$  mcg/mL (this breakpoint also can be applied to cats for uncomplicated infections). For cattle pathogens, use a break point of  $\leq 0.25$  mcg/mL. For equine respiratory pathogens (streptococci), use a break point of  $\leq 0.25$  mcg/mL.

## Formulations

- Amoxicillin is available in 50-, 100-, 150-, 200-, 400-, 500- and 875-mg tablets and 250- and 500-mg capsules (human preparations). Chewable tablets are available in sizes of 125-, 200-, 250-, and 400-mg.

- Amoxicillin trihydrate is available in 50-, 100-, 200-, and 400-mg tablets; 50-mg/mL amoxicillin trihydrate oral suspension; and 100- or 250-mg/mL amoxicillin trihydrate for injection.

### Stability and Storage

Store in a tightly sealed container at room temperature. Oral liquid suspensions are stable for 14 days. Other formulations should be protected from moisture. Optimum stability is at pH 5.8-6.5. Above this pH, hydrolysis occurs.

### Small Animal Dosage

#### Dogs and Cats

- 6.6-20 mg/kg q8-12h PO.

### Large Animal Dosage

#### Calves

- Nonruminating: 10-22 mg/kg q8-12h PO.

#### Cattle and Horses

- 6.6-22 mg/kg q8-12h PO (suspension). Note: Oral doses in large animals are not well absorbed (except in foals), and amoxicillin is generally not administered via this route.

### Regulatory Information

Withdrawal time: (Cattle only) 25 days for meat, 96 hours for milk. Amoxicillin intramammary infusion: withdrawal time 12 days for meat, 60 hours for milk.

## Amoxicillin and Clavulanate Potassium

ah-mox-ih-sill'in and klav-yoo-lan'ate poe-tah'see-um

**Trade and other names:** Clavamox (veterinary preparation) and Augmentin (human preparation)

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Beta-lactam antibiotic + beta-lactamase inhibitor (clavulanate potassium). Amoxicillin activity and spectrum are as described earlier. Clavulanate has no antibacterial effects alone, but it is a strong inhibitor of the beta-lactamase enzyme that causes resistance among gram-positive and gram-negative bacteria. By adding clavulanate to amoxicillin, the spectrum is extended to include beta-lactamase-producing strains of *Staphylococcus* (non-methicillin resistant) and many strains of gram-negative bacilli. However, unless treating uncomplicated lower urinary tract infections, many of the Enterobacteriaceae are resistant to typical doses of amoxicillin-clavulanate.

### Indications and Clinical Uses

Amoxicillin + clavulanate is a broad-spectrum antibacterial drug used for skin and soft tissue infections, UTIs, wound infections, and respiratory infections. It is indicated for treatment of bacterial infections (gram positive and gram negative) that may otherwise be resistant to amoxicillin due to bacterial beta-lactamase production.

## Precautionary Information

### Adverse Reactions and Side Effects

It is usually well tolerated. Allergic reactions are possible. Diarrhea is common with oral doses and has also caused vomiting in some animals. As the dose of clavulanate increases because of a high proportion of clavulanate in some formulations, vomiting is more likely.

### Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs. Oral administration to horses and ruminants may produce diarrhea.

### Drug Interactions

No drug interactions are reported in animals.

## Instructions for Use

Dose recommendations vary depending on the susceptibility of bacteria and location of infection. Generally, more frequent or higher doses are needed for gram-negative infections. It has been the experience of some dermatologists that an oral dose of double the manufacturer's recommendation should be used for treating skin infections (i.e., 25 mg/kg q12h). Oral human dose forms are sometimes substituted for veterinary drugs. Note that veterinary dose formulations contain amoxicillin and clavulanate in a 4:1 ratio. Human dose forms (Augmentin) contain these drugs in ratios of 2:1 to as high as 7:1.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 0.25/0.12$  mcg/mL for staphylococci, streptococci, *E. coli*, and *Pasteurella multocida*. (The “/” distinguishes the amoxicillin from the clavulanate concentrations.) When treating an uncomplicated lower urinary tract infection, a susceptibility breakpoint is  $\leq 8/4$  mcg/mL.

## Formulations

- Amoxicillin + clavulanate is available in veterinary dose form: 62.5-, 125-, 250-, and 375-mg tablets and 62.5-mg/mL suspension in a ratio of amoxicillin/clavulanate of 4:1. Amoxicillin + clavulanate is available in human dose form: 250/125-, 500/125-, and 875/125-mg tablets. Amoxicillin + clavulanate is available in 125/31.25-, 200/28.5-, 250/62.5-, and 400/57-mg chewable tablets and oral suspension 125/31.25, 200/28.5, 250/62.5, and 400/57 mg per 5 mL.

## Stability and Storage

Store in a tightly sealed container, protected from light, and below 24°C. Avoid exposure to humidity or moisture. Reconstituted oral products are stable for 10 days. Clavulanate is particularly unstable in compounded formulations and compounded products can exhibit a dramatic loss of potency, particularly in aqueous suspensions with acidic pH.

## Small Animal Dosage

### Dogs

- 12.5-25 mg/kg q12h PO. (Dose is based on combined ingredients: amoxicillin and clavulanate.)

### Cats

- 62.5 mg/cat q12h PO. Consider administering these doses every 8 hours for gram-negative infections.

## Large Animal Dosage

- Amoxicillin + clavulanate is only available in an oral formulation. Because these components are not absorbed orally in large animal species, this drug is not recommended.

## Regulatory Information

No regulatory information is available. However, it is anticipated that withdrawal times will be similar to those of amoxicillin.

## Amphotericin B

am-foe-tare'ih-sin

**Trade and other names:** Fungizone (traditional formulation) and liposomal forms of Amphotec, ABLC, ABCD, Abelcet, and AmBisome

**Functional classification:** Antifungal

## Pharmacology and Mechanism of Action

Antifungal drug. Amphotericin B is a fungicidal agent for systemic fungi. Amphotericin B binds to ergosterol in the fungal cell membrane, producing a loss of membrane integrity, leakiness, and cell death. Amphotericin is active against most fungi and some protozoa. There is a conventional formulation of amphotericin B deoxycholate that has been used most often in veterinary medicine. It is the least expensive but the most toxic. Lipid formulations of amphotericin B are now available. They are widely used in people but have not gained widespread use in veterinary medicine because of their high cost. The advantage of liposomal formulations over the traditional formulations is that they are less toxic. These new formulations are lipid-based complexes or cholesteryl complexes of amphotericin B that allow higher doses to be administered with less nephrotoxicity. Amphotericin B lipid complex (Abelcet, ABLC) is a suspension of amphotericin B complexed with two phospholipids at a concentration of 100 mg/20 mL. This formulation was shown to be safe and effective for treating blastomycosis in dogs at a cumulative dose of 8-12 mg/kg by administering 1 mg/kg every other day. Amphotericin B cholesteryl sulfate complex (Amphotec, ABCD) is a colloidal dispersion of amphotericin B. It has been effective in studies in which it was administered at doses higher than the traditional amphotericin B formulation. The liposomal complex of amphotericin B (AmBisome) is a unilaminar liposomal formulation. When reconstituted, it produces small vesicles of encapsulated amphotericin B. This formulation has been used safely and effectively in some dogs for blastomycosis.

## Indications and Clinical Uses

Amphotericin B is indicated in patients with a variety of systemic mycoses. It is used to treat blastomycosis, coccidioidomycosis, and histoplasmosis. It also has been used to treat leishmaniasis in dogs. It may be administered for treatment of aspergillosis, but this is not a common use in veterinary medicine, and some species of *Aspergillus* are resistant.

## Precautionary Information

### Adverse Reactions and Side Effects

Amphotericin B produces a dose-related nephrotoxicity. It also produces fever, phlebitis, and tremors. Renal toxicity is dose dependent and cumulative. It is more likely when cumulative doses approach or exceed 6 mg/kg. With repeated

use, amphotericin B can cause renal potassium wasting because of loss of potassium in the collecting duct.

### **Contraindications and Precautions**

Do not use in patients who have renal disease or where renal clearance is not known. Do not use in dehydrated animals or animals with electrolyte imbalances.

### **Drug Interactions**

When preparing IV solution, do not mix amphotericin B with electrolyte solutions; instead, use 5% dextrose in water. Nephrotoxicity is increased when administered with aminoglycosides.

## **Instructions for Use**

Administer IV via slow infusion diluted in 5% dextrose in water and monitor renal function closely. Administer sodium chloride fluid loading IV to patients before therapy to decrease risk of renal toxicosis. One study administered amphotericin B subcutaneously (*Aust Vet J*, 73: 124, 1996). Amphotericin B has been mixed as a solution of amphotericin B (one vial of 50 mg) with 40 mL of sterile water and 10 mL of Intralipid 10% (soybean oil). Doses of this mixture of 1-2 mg/kg have been used for treating systemic leishmaniasis. For other indications, this mixture has been administered at a dose of 1-2.5 mg/kg two times per week for 8-10 treatments. This liposomal complex of amphotericin B was used in a study for treatment of canine *Leishmania infantum* at a dose of 3-3.3 mg/kg. Although there was rapid clinical improvement, dogs remained positive for leishmaniasis. When administering proprietary forms of liposomal amphotericin B, follow instructions on label carefully. For administration of Abelcet, dilute in 5% dextrose to 1 mg/mL has been infused over 1-2 hours.

For intrathecal use, use the conventional formulation only. Start with 0.05 (total dose) every 48 hours, and increase to 0.1 and 0.2 mg (total dose) if the animal tolerates it well. Prepare intrathecal solution with a 5 mg/mL solution in sterile water, further diluting to 0.25 mg/mL by adding 1 mL (5 mg) of the solution to another 19 mL of 5% dextrose and inject directly intrathecally.

## **Patient Monitoring and Laboratory Tests**

Monitor renal function closely during treatment. After treatment, many animals will have an elevated creatinine and BUN. Persistent azotemia may be a cause for discontinuation of treatment and replacement with another antifungal agent. Hypokalemia and hypomagnesemia may occur during use because of renal tubular acidosis.

## **Formulations**

- The conventional form of amphotericin B is available in a 50-mg injectable vial. Liposomal forms are available as 50- and 100-mg injectable vial (Amphotec; lipid complex). Amphotericin B phospholipid complex (Abelcet) is available in a 100mg vial.

## **Stability and Storage**

Stable if stored in original vial. Amphotericin B for IV infusion will react with light and should be protected from light during infusions. Store reconstituted solutions in refrigeration. However, unrefrigerated solutions may be stable for up to 1 week. Optimum pH is 6-7.

## **Small Animal Dosage**

### **Dogs**

- Conventional formulation: 0.5 mg/kg q48 h IV (slow infusion) to a cumulative dose of 4-8 mg/kg. The liposomal formulations are administered at a dose of 3 mg/kg/day at a rate of more than 60-120 minutes for up to 9-12 treatments.

This dose may be administered three times per week, rather than every day. A goal for the total cumulative dose for liposomal formulations is 12-36 mg/kg.

- Intrathecal use: See previous instructions. Start with 0.05 (total dose) every 48 hours, and increase to 0.1 and 0.2 mg (total dose).
- Subcutaneous dose: 0.5-0.8 mg/kg diluted in 500 mL of 0.45% saline and 2.5% dextrose solution for dogs under 20 kg, and in 1000 mL for dogs greater than 20 kg. Drug concentration in fluid should not exceed 20 mg/L. Administer this dose 2 or 3 times per week SQ. Major complication from this method is sterile abscess at site of injection.

#### Cats

- Cats have received similar regimens to those used for dogs (e.g., 0.25 mg/kg conventional formulation). However, many clinicians will start with lower doses in cats. For liposomal formulations in cats, use 1 mg/kg IV three times per week for up to 12 treatments.

### Large Animal Dosage

#### Horses

- 0.3 mg/kg IV on day 1, followed by 3 consecutive days and repeat after a 24-48-hour drug-free interval. High cost of treatment has prevented common usage in horses.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Ampicillin, Ampicillin Sodium

am-pih-sill'in

**Trade and other names:** Omnipen, Principen, Totacillin, and Polycillin (human preparations); Omnipen-N, Polycillin-N, and Totacillin-N (injectable preparations); and Amp-Equine and Ampicillin trihydrate (Polyflex), and Amp-Tab (veterinary preparations)

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Ampicillin inhibits bacterial cell wall synthesis. Ampicillin has a narrow spectrum of activity that is similar to that of amoxicillin. Ampicillin generally has a spectrum of activity that includes streptococci, non-beta-lactamase-producing staphylococci, and other gram-positive cocci and bacilli. Many staphylococci are resistant due to beta-lactamase production. Most enteric gram-negative bacilli of the Enterobacteriaceae are resistant. Susceptible gram-negative bacteria include some species of *Proteus*, *Pasteurella multocida*, and *Histophilus*. Resistance among gram-negative bacteria is common.

Pharmacokinetics of ampicillin indicated that the half-life is approximately 1-1.5 hours in most animals. Half-life in horses is 0.6-1.5 hours after IV administration but longer after IM injection. When the trihydrate formulation is injected IM, it produces a lower peak concentration but a longer half-life of 6.7 hours in cattle. Volume of distribution in most species is approximately 0.2 L/kg. Systemic clearance is approximately 3-5 mL/kg/min in most animals. Oral absorption is less than 50% in dogs and cats and less than 4% in horses.

## Indications and Clinical Uses

Ampicillin is indicated in patients with infections caused by susceptible bacteria, such as skin and soft tissue infections, UTIs, and pneumonia. Gram-positive bacteria (except beta-lactamase-producing strains of *Staphylococcus*) are usually susceptible. However, infections caused by most gram-negative bacteria (except *Pasteurella*) are usually resistant.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects of penicillin drugs are most commonly caused by drug allergy. This can range from acute anaphylaxis when administered IV to other signs of allergic reaction when other routes are used. When used for prophylaxis during surgery, ampicillin can be administered IV to anesthetized patients without affecting cardiovascular parameters. Diarrhea is possible when administered orally, especially with high doses.

#### Contraindications and Precautions

Use cautiously in animals allergic to penicillinlike drugs. Ampicillin contains 3 mEq of sodium per gram. Rapid IV bolus injection can produce CNS excitement and convulsive seizures.

#### Drug Interactions

Do not mix in vials with other drugs.

## Instructions for Use

Dose requirements vary depending on susceptibility of bacteria. It is absorbed approximately 50% less compared to amoxicillin when administered orally. More frequent administration may be needed, and higher doses may be required for gram-negative bacilli and enterococci.

When preparing injectable solutions, the stability is dependent on the concentration. Concentrated solutions (250 mg/mL) should be injected within 1 hour of reconstitution either IM, SQ, or slowly (over 3 minutes) IV. Less concentrated solutions prepared in IV fluids (e.g., 30 mg/mL) are stable for longer periods. See “[Stability and Storage](#)” section for more detail.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: For testing for susceptibility, CLSI break point for sensitive organisms is  $\leq 0.25$  mcg/mL for staphylococci, streptococci, and gram-negative bacilli. For canine urinary tract pathogens, use a break point of  $\leq 8$  mcg/mL. For cattle pathogens, use a break point of  $\leq 0.25$  mcg/mL. For equine respiratory pathogens (streptococci), use a break point of  $\leq 0.25$  mcg/mL.

## Formulations

- Ampicillin is available in 125-, 250- and 500-mg capsules and 125-, 250-, and 500-mg vials of ampicillin sodium. Amp-Equine is available in 1- and 3-gram vials for injection. (However, this formulation has been discontinued by some suppliers.) Ampicillin trihydrate suspension (Polyflex) is available in 10- and 25-g vials for injection, and when reconstituted, each milliliter contains ampicillin trihydrate equivalent to 50, 100, or 250 milligrams of ampicillin.
- Although 1-, 2-, and 10-gram vials are primarily for IV use, they may be administered IM when the 250- and 500-mg vials are unavailable. In such instances, dissolve these vials in 3.5 or 6.8 mL sterile water, respectively (resulting concentration is 250 mg/mL). When using 1- or 2-gram vials for IV administration, dissolve 7.4 or 14.8 mL sterile water and administer over 15 minutes.

## Stability and Storage

Store in a tightly sealed container at room temperature. After reconstitution of ampicillin sodium, stability is concentration dependent. After reconstitution with sterile water at a concentration of 250 mg/mL, it is stable for 1 hour at room temperature. If diluted to a concentration of up to 30 mg/mL using 0.9% saline or lactated Ringer's solution (e.g., in IV fluids), stability is maintained for 8 hours at room temperature. In refrigerated temperatures, when reconstituted to 30 mg/mL, it is stable for 48 hours in sterile water, or 24 hours in sodium chloride or Ringer's solution. At 20 mg/mL, it is stable for 72 hours in sterile water, or 48 hours in sodium chloride. If this concentration is prepared in 5% dextrose in water, stability is maintained for only 1 hour. Oral suspensions are stable for 14 days if refrigerated. Ampicillin trihydrate for injection is stable for 12 months refrigerated and 3 months at room temperature. Other formulations should be protected from moisture. Optimum stability is at pH 5.8. Above this pH, hydrolysis occurs.

## Small Animal Dosage

### Dogs and Cats

- 10-20 mg/kg q6-8h IV, IM, or SQ or 20-40 mg/kg q8h PO. Doses as high as 100 mg/kg have been used for some resistant infections such as those caused by enterococci.

### *Ampicillin Trihydrate*

#### Dogs

- 10-50 mg/kg q12-24h IM or SQ.

#### Cats

- 10-20 mg/kg q12-24h IM or SQ.

## Large Animal Dosage

### Horses

- 6.6 mg/kg up to 10-20 mg/kg q6-8h IM or IV.
- Refractory infections: up to 25-40 mg/kg q6-8h.

### Cattle and Calves

### *Ampicillin Trihydrate*

- 4.4 to 11 mg/kg q24h IM.

## Regulatory Information

Cattle withdrawal time: 6 days for meat; 48 hours for milk (at 6 mg/kg).

Pig withdrawal time: In Canada, 6 days.

## Ampicillin + Sulbactam

am-pih-sill'in + sul-bak'tam

**Trade and other names:** Unasyn

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

The ampicillin component has the same spectrum and mechanism of action as described previously. This formulation contains ampicillin plus a beta-lactamase inhibitor (sulbactam). Sulbactam has similar activity as clavulanate (ingredient in



## 46 Ampicillin + Sulbactam

amoxicillin-clavulanate), but it is not as active as clavulanate against some gram-negative beta-lactamase enzymes (e.g., TEM). Because of the addition of sulbactam, it has a broader spectrum of activity than ampicillin alone. The spectrum includes beta-lactamase-producing strains of *Staphylococcus* and gram-negative bacilli. However, many gram-negative bacteria of the Enterobacteriaceae may be resistant.

### Indications and Clinical Uses

This combination is indicated for general bacterial infections. It has been used for acute infections such as pneumonia, sepsis, and prophylaxis in patients with neutropenia. Because of the addition of sulbactam, it has a broader spectrum than ampicillin alone. Therefore it is used for treating infections for which ampicillin resistance may be expected. It should be recognized that many gram-negative bacilli (e.g., Enterobacteriaceae) have MIC values that are in the “resistant” range for ampicillin-sulbactam. Therefore, when selecting an injectable penicillin derivative in combination with a beta-lactamase inhibitor, piperacillin-tazobactam should be considered. Ampicillin-sulbactam can only be administered by injection. For oral use, amoxicillin-clavulanate (e.g., Clavamox and Augmentin) may be used as an alternative.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects of penicillin drugs are most commonly caused by drug allergy. This can range from acute anaphylaxis when administered to other signs of allergic reaction when other routes are used.

#### Contraindications and Precautions

Use cautiously in animals allergic to penicillinlike drugs.

#### Drug Interactions

Do not mix in vials with other drugs.

### Instructions for Use

Dosage recommendations vary depending on the susceptibility of bacteria and location of infection. Generally, more frequent or higher doses are needed for gram-negative infections. When preparing injectable solutions, the stability is dependent on the concentration. Concentrated solutions (250 mg/mL) should be injected within 1 hour of reconstitution either IM, SQ, or slowly (over 3 minutes) IV. Vials for IM use may be reconstituted in lidocaine hydrochloride to decrease pain from injection. Less concentrated solutions prepared in IV fluids (e.g., 45 mg/mL) are stable for longer periods. See “[Stability and Storage](#)” section for more detail.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 8/4$  mcg/mL for staphylococci and gram-negative bacilli, based on the human breakpoint. (The “/” distinguishes the ampicillin from the sulbactam concentrations.) However, CLSI has lower breakpoints for amoxicillin/clavulanate in dogs and cats and it is possible that the ampicillin/sulbactam break point should be lower.

### Formulations

- Ampicillin + sulbactam is available in a 2:1 combination for injection and 1.5- and 3-g vials.

### Stability and Storage

Store vial in a tightly sealed container at room temperature. Vials may be reconstituted with sterile water for immediate use at an ampicillin concentration of 250 mg/mL. The vial should be used within 1 hour of reconstitution. When reconstituted vial is

diluted with sterile water or 0.9% sodium chloride at a concentration of 45 mg/mL, stability is maintained for 8 hours at room temperature and 48 hours if refrigerated. Stability is maintained for 8 hours at room temperature and 24 hours refrigerated if lactated Ringer's solution is used. Optimum stability is at pH 5.8. Above this pH, hydrolysis occurs.

### Small Animal Dosage

#### Cats and Dogs

- Doses are similar to those used for ampicillin (when dosed according to ampicillin component) 10-20 mg/kg q8h IV or IM.

### Large Animal Dosage

#### Horses and Ruminants

- Doses used should be same as for ampicillin component.
- 6.6 mg/kg up to 10-20 mg/kg q6-8hr, IM or IV.

### Regulatory Information

Withdrawal time exists for ampicillin but not sulbactam. Because sulbactam has a similar half-life and presents little risk for toxicity, the withdrawal times listed for ampicillin are suggested.

Cattle withdrawal time: 6 days for meat; 48 hours for milk (at 6 mg/kg).

Pig withdrawal time: In Canada, 6 days.

## Amprolium

am-proe'lee-um

**Trade and other names:** Amprol and Corid

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Antiprotozoal drug. This drug is a vitamin B<sub>1</sub> or thiamine structural analogue. Amprolium antagonizes thiamine in parasites and is used for treatment of coccidiosis.

### Indications and Clinical Uses

Amprolium is used to control and treat coccidiosis in calves, sheep, goats, puppies, and birds. It is administered orally, often mixed with food.

### Precautionary Information

#### Adverse Reactions and Side Effects

Toxicity is observed only at high doses. Central nervous system signs are caused by thiamine deficiency, which may be reversed by adding thiamine to the diet.

#### Contraindications and Precautions

Do not administer to debilitated animals.

#### Drug Interactions

No drug interactions are reported in animals.

### Instructions for Use

Usually administered as feed additive to livestock. For dogs, 30 mL of 9.6% amprolium has been added to 3.8 L of drinking water for control of coccidiosis.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Amprolium is available in 9.6% (9.6 g/100 mL) oral solution and a soluble powder in a 22.6-g packet.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- Treatment of coccidiosis: Add 1.25 g of 20% amprolium powder to daily feed or 30 mL of 9.6% amprolium solution to 3.8 L of drinking water for 7 days.

## Large Animal Dosage

### Calves

- Prevention of coccidiosis: 5 mg/kg q24h for 21 days.
- Treatment of coccidiosis: 10 mg/kg q24h for 5 days PO.

## Regulatory Information

Withdrawal time for cattle (meat): 24 hours before slaughter.

A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal.

## Apomorphine Hydrochloride

ah-poe-mor'feen hye-droe-klor'-ide

**Trade and other names:** Apokyn and generic brands

**Functional classification:** Emetic

## Pharmacology and Mechanism of Action

Emetic drug. Apomorphine is a potent lipophilic agent that crosses the blood–brain barrier and stimulates dopamine (D<sub>2</sub>) or chemoreceptor trigger zone (CTZ) receptors in the vomiting center. It promptly causes vomiting in dogs. Although it is easily absorbed from mucosal surfaces (e.g., conjunctiva of the eye), it is not absorbed orally because of first-pass effects.

## Indications and Clinical Uses

Apomorphine is indicated for inducing emesis in animals that have ingested toxic agents. After subcutaneous administration, the onset of effect is 10 minutes or shorter. It is promptly effective for inducing vomiting in dogs but less so in cats. Apomorphine also is absorbed from mucosal administration after applying to the conjunctiva of the eye. Xylazine often is a more reliable emetic in cats. In dogs 3% hydrogen peroxide (2.2 mL/kg) was equally effective for inducing emesis. The dose of 3% hydrogen peroxide is typically 2.2 mL/kg (1 mL per pound).

## Precautionary Information

### Adverse Reactions and Side Effects

Apomorphine produces emesis before serious adverse effects can occur, but at higher doses (0.1 mg/kg) sedation can occur, which can mask the signs of some toxic agents. The hydrochloride salt of this formulation has a pH of 3-4 and can be irritating to the ocular conjunctival membranes. At high doses (1 mg/kg), excitement can occur, possibly via stimulation of dopamine (D<sub>1</sub> and D<sub>2</sub>) receptors.

### Contraindications and Precautions

Apomorphine also may decrease vomiting stimulus in vomiting center; therefore, if the initial dose is not effective, emetic effects may be blocked during later attempts to induce vomiting. Use cautiously in cats that may be sensitive to opiates. (Xylazine is a more effective emetic agent in cats.)

### Drug Interactions

No drug interactions are reported in animals. However, some drugs will diminish the emetic action of apomorphine (e.g., acepromazine, atropine, and other antiemetics).

## Instructions for Use

Consult local poison center or pharmacist for availability. Apomorphine should be available in most emergency practices for prompt treatment of poisoning. Apomorphine can be administered IM, SQ, or to the mucosa (e.g., in the conjunctival sac of the eye). In dogs, vomiting should occur within 3-10 minutes after administration. Limit administration to once.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. If used to induce vomiting from a toxicant, monitor for signs of toxicity because vomiting is able to eliminate less than half of the ingested toxicant.

## Formulations

- Apomorphine is available in 6-mg tablets that can be hydrolyzed prior to use or is available in a 10-mg/mL concentration in a 2-mL ampule or 3-mL preloaded syringes. It has also been prepared by compounding pharmacists by mixing 20 mg apomorphine in a sterile vial with 4.4 mL sterile water to make a solution of 5 mg/mL. From this solution, drops may be added to eye to induce vomiting.

## Stability and Storage

Solutions decompose when exposed to air and light. A green color indicates decomposition. Store in a tightly sealed container at room temperature.

## Small Animal Dosage

### Dogs and Cats

- 0.03-0.05 mg/kg IV or IM.
- 0.1 mg/kg SQ.
- Dissolve 6-mg tablet in 1-2 mL of 0.9% saline solution and instill directly in conjunctiva of eye. After animal vomits, the conjunctiva may be rinsed of residual drug with an eye wash solution.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 1

## Aprepitant

ap-reh'pīh-tant

**Trade and other names:** Emend**Functional classification:** Antiemetic

### Pharmacology and Mechanism of Action

Aprepitant is a centrally acting antiemetic. Aprepitant is a substance P/neurokinin 1 (NK<sub>1</sub>) receptor antagonist, similar to maropitant (Cerenia). It is used primarily with drugs known to be highly emetic, such as cisplatin. This drug is effective because chemotherapy drugs and other emetic stimuli release NK<sub>1</sub>, which is highly emetic. It also blocks vomiting from other stimuli. The use in small animals has been somewhat limited because of the high expense and limited formulations for animals. In dogs, aprepitant is extensively metabolized after administration.

### Indications and Clinical Uses

Aprepitant is an effective antiemetic for people, particularly when used to treat vomiting associated with cancer chemotherapy. It may be used with corticosteroids (dexamethasone) and serotonin (5HT<sub>3</sub>) antagonists. However, despite its broad effects to decrease vomiting in people, there are no reports of effective use in dogs or cats. Instead, a similar-acting drug, maropitant (Cerenia), is used in dogs and cats and produces similar antiemetic effects.

### Precautionary Information

#### Adverse Reactions and Side Effects

There are no reported adverse effects in animals.

#### Contraindications and Precautions

No contraindications reported for animals.

#### Drug Interactions

Drug interactions are possible because aprepitant is both an inducer and inhibitor of cytochrome P450 enzymes. Potent inhibitors of cytochrome P450 can potentially affect aprepitant clearance.

### Instructions for Use

Use in patients refractory to other antiemetic drugs. It may be combined with other antiemetics.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Aprepitant is available in 80- and 125-mg capsules and as Fosaprepitant dimeglumine in a 150-mg vial for IV use.

### Stability and Storage

Do not crush or mix capsules. Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- Start with 1 mg/kg q24h PO and increase to 2 mg/kg in refractory patients.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Ascorbic Acid

ah-skor'bik ass'id

**Trade and other names:** Vitamin C and sodium ascorbate. Many brand names are available.

**Functional classification:** Vitamin

## Pharmacology and Mechanism of Action

Ascorbic acid is vitamin C. It is an important cofactor in a variety of metabolic functions.

## Indications and Clinical Uses

Ascorbic acid is used to treat vitamin C deficiency and occasionally used as a urine acidifier. Dogs are capable of synthesizing vitamin C, but it is used as a supplement to improve health and performance. There are insufficient data to show that ascorbic acid is effective for preventing cancer, treating infectious diseases, or preventing cardiovascular disease.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. High doses may increase the risk of oxalate urolith formation.

### Contraindications and Precautions

No contraindications reported for animals.

### Drug Interactions

No drug interactions are reported in animals.

## Instructions for Use

Not necessary to supplement in animals with well-balanced diets. However, high doses have been used as adjunctive treatment for some diseases. Evidence shows that at doses of 15 and 50 mg/kg in dogs, the increase in absorption was nonlinear. Therefore higher doses may not produce proportionately higher blood levels to the lower doses. Comparison of crystalline ascorbic acid and the vitamin C product, Ester-C, produced similar levels of vitamin C in the plasma.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Ascorbic acid is available in tablets of various sizes and injections. Typically the injection form is 250 mg sodium ascorbate/mL. The formulation of Ester-C appears to be absorbed similarly to the crystalline form of vitamin C.

## 52 Asparaginase (L-Asparaginase)

### Stability and Storage

Light sensitive. It will oxidize, darken, and decompose when exposed to air and light. The injectable solution in a vial may build up pressure with storage, which may be decreased by storing in a refrigerator. Otherwise, store at room temperature protected from light.

### Small Animal Dosage

#### Dogs and Cats

- Dietary supplementation: 100-500 mg/animal/day PO.
- Urinary acidification: 100 mg/animal q8h PO. Injectable dose ranges from 1-10 mL (250 mg per mL), depending on size of animal, IM or IV.
- For treatment of oxidative stress: Dogs: 500-1000 mg per dog q24h, PO; Cats: 125 mg per cat, PO, q12h.

#### Guinea Pigs

- 16 mg/kg twice weekly IM, to treat vitamin deficiency.

### Large Animal Dosage

#### Large Animals

- Vitamin C supplementation: 1-10 mL IM or IV. Repeat daily as needed.
- 1-2 g q24h PO.

### Regulatory Information

Withdrawal time: 0 days for all animals intended for food.

## Asparaginase (L-Asparaginase)

ah-spar'a-jin-aze

**Trade and other names:** Elspar and Asparaginase

**Functional classification:** Anticancer agent

### Pharmacology and Mechanism of Action

Anticancer agent. Neoplastic cells are deficient in asparagine synthase and require extracellular asparagine for DNA and RNA synthesis. L-asparaginase destroys asparagine. Normal cells are capable of synthesizing their own asparagine, but certain malignant cells, especially malignant lymphocytes, are not. Therefore asparagine is an essential amino acid for cancer cell survival, particularly malignant lymphocytes. Because cancer cells in patients treated with L-asparaginase are depleted of asparagine, this treatment interferes with DNA, RNA, and protein synthesis in cancer cells. It is specific for the G1 phase of the cell cycle. In dogs it has a long half-life of 1-2 days.

### Indications and Clinical Uses

Asparaginase has been used in some lymphoma protocols and has been effective for melanoma and mast cell tumors. It has been administered IV, IM, or SQ, but results of one study favored IM administration over SQ administration. In cats it also has been used in combination cancer protocols.

### Precautionary Information

#### Adverse Reactions and Side Effects

The most common adverse effect is hypersensitivity (allergic) reactions. Asparaginase is a foreign bacterial protein and can cause allergic reactions. Animals have developed

hypersensitivity after repeated injections. Hepatotoxic reactions, pancreatitis, and hyperglycemia also have been reported. In some dogs, although rare, increases in ammonia are possible that can lead to hyperammonemic encephalopathy.

### Contraindications and Precautions

Do not use in animals with known sensitivity (allergic reaction).

### Drug Interactions

No drug interactions are reported in animals. It has been used with other anticancer drugs.

## Instructions for Use

Asparaginase is usually used in combination with other drugs in cancer chemotherapy protocols (e.g., doxorubicin). Studies have shown that intramuscular dosing is more effective than subcutaneous dosing in dogs with lymphoma. Asparaginase has minimal effect on the bone marrow; therefore it can be used in combination with other myelosuppressive drugs in a protocol. Although it has been used in anticancer protocols, it has shown no benefit when added to cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) protocols for lymphoma. Tumor cells can develop resistance by developing a capacity to synthesize asparagine. In cats, it has been used in combination protocols at a dose of 400 units per kg SQ on day one of protocols combined with doxorubicin.

## Patient Monitoring and Laboratory Tests

Monitoring CBC during chemotherapy is recommended.

## Formulations

- Asparaginase is available in 10,000 units per vial for injection. (Distribution of this drug to veterinarians by the manufacturer may be limited.)

## Stability and Storage

Stable if stored in manufacturer's original vial.

## Small Animal Dosage

### Dogs

- 400 units/kg SQ or IM, weekly.
- 10,000 units/m<sup>2</sup> weekly SQ or IM for 3 weeks.

### Cats

- 400 units/kg weekly SQ or IM.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals that produce food because it is an anticancer agent.

## Aspirin

as'pir-in

**Trade and other names:** ASA, acetylsalicylic acid, Bufferin, Ascriptin, and many generic brands

**Functional classification:** Nonsteroidal anti-inflammatory



## Pharmacology and Mechanism of Action

Nonsteroidal anti-inflammatory drug (NSAID). Anti-inflammatory action is caused by inhibition of prostaglandins. Aspirin binds irreversibly to the cyclo-oxygenase (COX) enzyme in tissues to inhibit synthesis of prostaglandins. At low doses it may be more specific for COX-1 than COX-2. The sensitivity of COX-1 over COX-2 is the explanation for low aspirin doses used as anti-platelet treatment. However in some animals, even low-dose aspirin does not inhibit platelet aggregation, possibly because COX-2 can be an additional source of thromboxane (TXA<sub>2</sub>). Anti-inflammatory effects are attributed to inhibition of COX, but other anti-inflammatory mechanisms—attributed to salicylates—may also contribute to the anti-inflammatory action, such as inhibition of NF kappa- $\beta$ . Pharmacokinetics are variable in animals with a half-life that ranges from 1 hour in horses, 6 hours in pigs, 8.5 hours in dogs, to 38 hours in cats.

## Indications and Clinical Uses

Aspirin is used as an analgesic, anti-inflammatory, and antiplatelet drug. At low doses, aspirin is a more specific COX-1 selective inhibitor and antiplatelet drug than other NSAIDs. Therefore low doses have been used in animals specifically to prevent thromboemboli formation. Low doses of aspirin are routinely used for antiplatelet therapy, but aspirin does not provide complete inhibition of platelet stimulation. Addition of other antiplatelet drugs such as clopidogrel (Plavix) provides more effective inhibition. Inhibition of platelets has been justified because in some diseases, platelets may become hyper-reactive, and release serotonin and other mediators that may exacerbate vascular diseases.

Aspirin has been used to prevent complications from heartworm disease (thromboemboli). However, there is no convincing evidence that there is a clinical benefit from this treatment. Some evidence indicates that aspirin may be contraindicated in heartworm disease.

In cats, exposure of feline platelets in vitro to aspirin can have an inhibitory effect. Platelets collected from cats ex vivo after treatment with aspirin (5 mg/kg) had decreased thromboxane production (TXA<sub>2</sub>) but platelet aggregation was not affected. Although aspirin has been available for many years, it is not registered by the Food and Drug Administration (FDA) for use in any species. There are no published controlled studies to document efficacy. Use of aspirin in animals is primarily based on empiricism rather than on published data.

## Precautionary Information

### Adverse Reactions and Side Effects

Narrow therapeutic index. High doses frequently cause vomiting. Other gastrointestinal effects can include ulceration and bleeding. Aspirin may inhibit platelets and increases risk of bleeding.

### Contraindications and Precautions

Cats are susceptible to salicylate intoxication because of slow clearance. Use cautiously in patients with coagulopathies because of platelet inhibition (e.g., von Willebrand disease). Do not administer to animals prone to gastrointestinal ulcers.

### Drug Interactions

Do not administer with other ulcerogenic drugs such as corticosteroids. Do not administer with other drugs that may cause coagulopathy and increase risk of bleeding problems.

## Instructions for Use

Analgesic and anti-inflammatory doses have primarily been derived from empiricism. Anti-platelet doses are lower because of potent and prolonged effect of aspirin on platelets. The dosing section lists “antiplatelet” doses for aspirin in dogs and cats, but the efficacy of

these doses has not been verified through clinical studies. Results from research animals have produced varied results. In some studies, 5-10 mg/kg was considered an antiplatelet dose for dogs, in other studies 1 mg/kg inhibited platelets in only one-third of dogs, and in research dogs, doses as low as 0.5 mg/kg q12h impaired platelet aggregation.

Aspirin is only available in oral form. Because it is a weak acid, it is ordinarily absorbed best in the acidic environment of the upper gastrointestinal tract; however, considerable absorption also takes place in the intestine. In dogs, enteric-coated aspirin reduces gastric irritation, but absorption from this form is erratic and often incomplete. Buffering does not affect absorption but may protect the stomach from injury when high doses are administered. Buffering has less of a beneficial effect when low doses are administered and is not expected to protect the stomach from the more serious effects of gastrointestinal ulceration, bleeding, and perforations.

### Patient Monitoring and Laboratory Tests

Monitor patients for signs of gastric upset, gastroduodenal ulcers, and bleeding. Effective plasma concentrations: 20-50 mcg/mL for pain and fever and 150-200 mcg/mL for inflammation. Aspirin decreased thyroid concentrations ( $T_4$ ,  $T_3$ , and  $fT_4$ ) in dogs after 2-4 weeks of dosing but returned to normal in 14 days.

### Formulations

- Aspirin is available in 81-mg (children's aspirin) and 325-mg tablets.
- For large animals, aspirin is available in 240-grain bolus (14,400 mg) and 3.9-, 15.6-, and 31.2-g tablets.

### Stability and Storage

Store in a tightly sealed container at room temperature. After exposure to moisture, it will decompose to acetic acid and salicylic acid. If stored at pH 7 at 25°C, it has a half-life of 52 hours.

### Small Animal Dosage

#### *Mild Analgesia*

##### Dogs

- 10 mg/kg q12h PO.

#### *Anti-inflammatory*

##### Dogs

- 20-25 mg/kg q12h PO.

#### *Antiplatelet*

##### Dogs

- Typical doses are in the range of 1-5 mg/kg, and usually 5-up to 10 mg/kg q24-48h PO. (Convincing evidence of an antiplatelet clinical benefit in dogs is lacking.)

##### Cats

- 10 mg/kg q48h PO.

##### Cats

- 10-20 mg/kg q48h PO.

##### Cats

- 80 mg/cat q48h PO. Doses have ranged from 5 mg per cat q72h, to 80 mg per cat (one tablet) q72h. No clinical studies have documented efficacy from either dose.

### Large Animal Dosage

#### Ruminants

- 100 mg/kg q12h PO. Doses as high as 333 mg/kg have been administered to cattle.

#### Swine

- 10 mg/kg q6-8h PO.

#### Horses

- 25-50 mg/kg q12h PO (up to 100 mg/kg PO, per day).

**Regulatory Information**

Extralabel use: Although considered extralabel in animals intended for food, consider a withdrawal time of at least 1 day for meat and 24 hours for milk.

RCI Classification: 4

**Atenolol**

(ah-ten'oe-lole)

**Trade and other names:** Tenormin

**Functional classification:** Beta-antagonist

**Pharmacology and Mechanism of Action**

Beta-adrenergic blocker. Relatively selective for beta<sub>1</sub>-receptor. Atenolol is a water-soluble beta blocker and relies on the kidneys for clearance. (By comparison, drugs such as propranolol and metoprolol are more lipophilic and rely on the liver for clearance.) In dogs and cats, oral absorption is 90%. In cats, the half-life is approximately 4-5 hours, with a peak concentration of 1.4-1.9 mcg/mL after a dose of 2.5 mg/kg.

**Indications and Clinical Uses**

Atenolol is one of the most commonly administered beta blockers for dogs and cats. Atenolol is used primarily as an antiarrhythmic or for other cardiovascular conditions in which it is needed to slow the sinus rate. In cats, this drug is commonly used to treat heart disease from cardiomyopathy or hyperthyroidism, but it should not be used as monotherapy to treat primary hypertension. Although it is commonly administered to cats with hypertrophic cardiomyopathy to improve clinical signs, it did not slow progression of the disease. In dogs it has been used for congenital cardiac conditions such as subaortic stenosis and pulmonary stenosis (0.5-1 mg/kg, q12h).

**Precautionary Information****Adverse Reactions and Side Effects**

Bradycardia and heart block are possible. Atenolol may produce bronchospasm in sensitive patients.

**Contraindications and Precautions**

Use cautiously in animals with airway disease, myocardial failure, and cardiac conduction disturbances. Use cautiously in animals with low cardiac reserve.

**Drug Interactions**

Use cautiously with other drugs that may decrease cardiac contraction or heart rate.

**Instructions for Use**

Atenolol is reported to be less affected by changes in hepatic metabolism than other beta blockers. Although not an FDA-approved drug for dogs and cats, dosing guidelines are based on published reports and experience of experts. In cats, amlodipine (calcium-channel blocker) may be used with atenolol to control hypertension. When administered as a transdermal gel to cats, it produced inconsistent and lower plasma concentrations compared to oral administration.

## Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and rhythm. Although plasma/serum concentrations are not typically monitored, a concentration above 0.26 mcg/mL has been proposed as a target threshold for effective adrenergic beta-receptor blockade.

## Formulations

- Atenolol is available in 25-, 50-, and 100-mg tablets. (Tablets can be split for small animals.)

## Stability and Storage

Store in a tightly sealed container at room temperature. Studies using a compounded flavored oral paste and oral suspension formulation for cats produced similar beta-adrenergic blocking effects as a commercial tablet (2.5 mg/kg). Stability studies indicate that extemporaneously prepared oral suspensions are stable for 14 days, and some compounded oral formulations have been stable for 60 days. Consult compounding pharmacist for beyond-use-day of prepared compounded formulations. Atenolol is water soluble.

## Small Animal Dosage

### Dogs

- 6.25-12.5 mg/dog q12-24h (or 0.25-1.0 mg/kg q12-24h) PO. Doses in dogs have been increased to 3 mg/kg q12-24h PO for some conditions.

### Cats

- 1-2 mg/kg q12h, PO. However, because of tablet size, a common dose is 6.25-12.5 mg/cat q12-24h PO (one-quarter or one-half tablet).

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Atipamezole Hydrochloride

ah-tih-pam'eh-zole hye-droe-klor'ide

**Trade and other names:** Antisedan

**Functional classification:** Anesthetic

## Pharmacology and Mechanism of Action

Alpha<sub>2</sub>-antagonist. It binds to alpha<sub>2</sub>-receptors to antagonize other drugs that act as agonists, such as dexmedetomidine, medetomidine, and xylazine. Other alpha<sub>2</sub>-antagonists include yohimbine, but atipamezole is more specific for the alpha<sub>2</sub>-receptor.

## Indications and Clinical Uses

Atipamezole is used to reverse alpha<sub>2</sub>-agonists such as dexmedetomidine (Dexdomitor), medetomidine (Domitor), detomidine, and xylazine. Arousal from sedation should occur within 5-10 minutes of injection. It also can be used to reverse sedation caused by amitraz intoxication. In horses, it provides a satisfactory, but incomplete reversal of detomidine.

## Precautionary Information

### Adverse Reactions and Side Effects

Atipamezole can cause initial excitement in some animals shortly after reversal. There may be a transient decrease in blood pressure after injection. In horses, it can produce a dose-dependent increase in sweating and hyperexcitability that resolved after 10-15 minutes.

### Contraindications and Precautions

No contraindications reported for animals.

### Drug Interactions

Atipamezole is an  $\alpha_2$ -antagonist. As such, it will antagonize other drugs that bind to the alpha-receptor and prevent their action. Such drugs that may be antagonized include xylazine, medetomidine, dexmedetomidine, romifidine, detomidine, and some  $\alpha_1$ -agonists.

## Instructions for Use

When used to reverse dexmedetomidine or medetomidine, inject the same volume of atipamezole as the volume of dexmedetomidine or medetomidine that was administered. The dose in horses (see below) has used a wide range. Typically, the higher dose is more effective for detomidine, but tolazoline antagonizes detomidine in horses more completely and hastens recovery better than atipamezole.

## Patient Monitoring and Laboratory Tests

Monitor cardiovascular status when using  $\alpha_2$ -agonists. Providing oxygen during recovery may help recovery from  $\alpha_2$ -agonists.

## Formulations

- Atipamezole is available in a 5-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

- Inject the same volume as used for dexmedetomidine or medetomidine. The range of doses (IM or IV) is 0.32 mg/kg for small animals (4 kg, or 8.8 pounds), 0.23 mg/kg for medium-sized animals (11 kg, or 24 pounds), and up to 0.14 mg/kg for large-sized animals (45 kg or 100 pounds).

## Large Animal Dosage

- Horses: The dose used in horses is 60-80 mcg/kg (0.06-0.08 mg/kg) IV, but has ranged up to 150 mcg/kg (0.15 mg/kg). Typically, 100 mcg/kg (0.1 mg/kg) IV is used to reverse detomidine.

## Regulatory Information

Do not administer to animals intended for food.

## Atovaquone

a-TOE-va-KWONE

**Trade and other names:** Mepron

**Functional classification:** Antibacterial, antiprotozoal

## Pharmacology and Mechanism of Action

Atovaquone is an antimicrobial agent, an analogue of ubiquinone, that inhibits mitochondrial transport in protozoa by targeting the cytochrome bc<sub>1</sub> complex. It also inhibits nucleic acid and adenosine triphosphate (ATP) synthesis in susceptible cells. Atovaquone is active against protozoa such as *Pneumocystitis*, for which it is used in people. In cats, it is used to treat *Cytauxzoon felis*. It may not eradicate *Cytauxzoon*, but it will decrease the parasite burden. In dogs, it has been used to treat *Babesia gibsoni*. For treating these infections in dogs and cats, it appears to have an additive or synergistic effect when combined with azithromycin. It is highly lipophilic. Oral absorption in animals is almost 50% but is increased with feeding. The half-life in people is very long (67-77 hours) but is not reported for animals.

## Indications and Clinical Uses

In people, atovaquone is an antiprotozoal that is primarily used in individuals who cannot tolerate sulfonamides. In animals, it has been used, often in combination with azithromycin, to treat refractory protozoan diseases and bloodborne pathogens.

### Precautionary Information

#### Adverse Reactions and Side Effects

One formulation (Malarone) also contains proguanil HCl. It may increase the risk of diarrhea in dogs when combined with proguanil. Otherwise, adverse effects have not been reported in animals. In people, adverse reactions consist of skin rash, cough, and diarrhea.

#### Contraindications and Precautions

Avoid use in pregnancy.

#### Drug Interactions

No drug interactions are reported in animals. In people, coadministration with rifampin will decrease effective concentrations.

## Instructions for Use

There has been only limited experience with use of atovaquone for treatment of infections in animals. A few clinical trials have shown efficacy when combined with azithromycin for treatment of protozoa infections.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Atovaquone is available as a 750-mg-per-5-mL liquid oral suspension (150 mg/mL). The 250-mg tablets have been discontinued.

## Stability and Storage

Store at room temperature protected from light. Do not freeze.

## Small Animal Dosage

### Cats

- 15 mg/kg q8h, PO, in combination with azithromycin (10 mg/kg q24h).

### Dogs

- 13.3 mg/kg q8h, PO for 10 days, usually in combination with azithromycin (10 mg/kg q24h, PO).

## Large Animal Dosage

### Large Animals

- No dose reported.

## Regulatory Information

There is no withdrawal time established for food animals.

## Atracurium Besylate

ah-tra'h-kyoor'ee-um bess'ih-late

**Trade and other names:** Tracrium

**Functional classification:** Muscle relaxant

## Pharmacology and Mechanism of Action

Neuromuscular blocking agent (nondepolarizing). Atracurium competes with acetylcholine at the neuromuscular end plate. It is used primarily during anesthesia or other conditions in which it is necessary to inhibit muscle contractions. It has a shorter duration of action than pancuronium.

## Indications and Clinical Uses

Atracurium is a paralytic agent used to paralyze skeletal muscle during surgery and mechanical ventilation.

## Precautionary Information

### Adverse Reactions and Side Effects

Atracurium produces respiratory depression and paralysis. Neuromuscular-blocking drugs have no effect on analgesia.

### Contraindications and Precautions

Do not use in patients unless it is possible to provide ventilation support. The action of neuromuscular-blocking agents may be antagonized by acetylcholinesterase inhibitors.

### Drug Interactions

Gentamicin (and possibly other aminoglycosides) potentiates neuromuscular blockade (gentamicin acts at the presynaptic site to decrease release of acetylcholine). No other drug interactions are reported in animals.

## Instructions for Use

Administer only in situations in which careful control of respiration is possible. Doses may need to be individualized for optimum effect. Do not mix with alkalinizing solutions or lactated Ringer's solution.

## Patient Monitoring and Laboratory Tests

Monitoring of respiratory and cardiovascular indices is critical during use. If possible, monitor oxygenation of patient during use.

## Formulations

- Atracurium is available in 10-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 0.2 mg/kg IV initially, then 0.15 mg/kg q30min.
- Constant-rate infusion: 0.3-0.5 mg/kg IV loading dose, followed by 4-9 mcg/kg/min.

## Large Animal Dosage

### Horses

- 0.05-0.07 mg/kg IV.

## Regulatory Information

Do not administer to animals intended for food.

## Atropine Sulfate

ah'troe-peen sul'fate

**Trade and other names:** Generic brands

**Functional classification:** Anticholinergic

## Pharmacology and Mechanism of Action

Anticholinergic agent (blocks acetylcholine effect at muscarinic receptors), parasympatholytic.

As an antimuscarinic agent, it blocks cholinergic stimulation and causes decrease in gastrointestinal motility and secretions, decrease in respiratory secretions, increased heart rate (antivagal effect), and mydriasis.

## Indications and Clinical Uses

Atropine is used primarily as an adjunct to anesthesia or other procedures to increase heart rate and decrease respiratory and gastrointestinal secretions. Atropine is the drug of choice to overcome excess vagal stimulation associated with some clinical conditions. Atropine is also used as an antidote for organophosphate intoxication.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects include xerostomia, ileus, constipation, tachycardia, and urine retention.

### Contraindications and Precautions

Do not use in patients with glaucoma, intestinal ileus, gastroparesis, or tachycardia.

Use high doses (e.g., 0.04 mg/kg) cautiously because it will increase oxygen demand.

### Drug Interactions

Do not mix with alkaline solutions. Atropine will antagonize the effects of any cholinergic drugs administered (e.g., metoclopramide).

## Instructions for Use

Atropine is used ordinarily as an adjunct with anesthesia or other procedures. Compared to lower doses, in dogs 0.06 mg/kg was more effective than 0.02 mg/kg. Atropine may be used during cardiac resuscitation; however, high doses may cause sustained tachycardia and increased myocardial oxygen demand. During cardiac resuscitation, doses of 0.04 mg/kg IV may be used, but for treating sinus bradycardia, consider lower doses of 0.01 mg/kg.

## Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and rhythm.



**Formulations**

- Atropine is available in 400-, 500-, and 540-mcg/mL injection and 15-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container at room temperature.

**Small Animal Dosage****Dogs**

- 0.02-0.04 mg/kg q6-8h IV, IM, or SQ (complete dose range has been from 0.01 mg/kg to 0.06 mg/kg, depending on the indication).
- Sinus bradycardia: 0.005-0.01 mg/kg, but for use during cardiopulmonary resuscitation (CPR) up to 0.04 mg/kg.

**Cats**

- 0.02-0.04 mg/kg q6-8h IV, IM, or SQ.

**Dogs**

- For organophosphate and carbamate toxicosis: 0.2-0.5 mg/kg as needed, IV, IM, or SQ.

**Cats**

- For organophosphate and carbamate toxicosis: 0.2-0.5 mg/kg as needed, IV, IM, or SQ.

**Large Animal Dosage**

Note that in large animals, atropine has a potent effect on inhibiting gastrointestinal motility.

**Horses**

- Antidote to organophosphates or cholinesterase inhibitors: 0.02-0.04 mg/kg IM or SQ, and repeat as needed.
- Recurrent airway obstruction (RAO): 0.022 mg/kg, once, IV.

**Pigs**

- Antidote to organophosphates or cholinesterase inhibitors: 0.1 mg/kg IV followed by 0.4 mg/kg IM.
- Anesthesia adjunct: 0.02 mg/kg IV or 0.04 mg/kg IM.

**Ruminants**

- Antidote to organophosphates or cholinesterase inhibitors: 0.1 mg/kg IV, followed by 0.4 mg/kg IM and repeat as needed.
- Anesthesia adjunct to prevent salivation: 0.02 mg/kg IV or 0.04 mg/kg IM.

**Regulatory Information**

Withdrawal time: None established in US. The manufacturer of large animal products lists 0 days for milk and meat; however, it is listed as 14 days for meat and 3 days for milk in the UK.

RCI Classification: 3

**Auranofin**

or-an'oe-fin

**Trade and other names:** Ridaura

**Functional classification:** Immunosuppressive

## Pharmacology and Mechanism of Action

Used for gold therapy (chrysotherapy). Mechanism of action is unknown but may relate to immunosuppressive effect on lymphocytes.

## Indications and Clinical Uses

Auranofin (gold therapy) is used primarily for immune-mediated diseases. It has been used with some success to control immune-mediated skin diseases, such as pemphigus and immune-mediated arthritis, but evidence of efficacy is lacking for small animal therapy. It has been observed by some clinicians that this product (oral) is not as effective as injectable products such as aurothioglucose.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects include dermatitis, nephrotoxicity, and blood dyscrasias.

#### Contraindications and Precautions

Do not use in animals with suppressed bone marrow or in animals already receiving bone marrow-suppressing agents.

#### Drug Interactions

No drug interactions are reported in animals.

## Instructions for Use

Use of this drug has not been evaluated in veterinary medicine. No controlled clinical trials are available to determine efficacy in animals.

## Patient Monitoring and Laboratory Tests

Monitor patient's CBC periodically because gold salts have caused blood dyscrasias.

## Formulations

- Auranofin is available in 3-mg capsules.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 0.1-0.2 mg/kg q12h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

## Aurothioglucose

or-oh-thye-oe-gloo'kose

**Trade and other names:** Solganal

**Functional classification:** Immunosuppressive

## **Pharmacology and Mechanism of Action**

Used for gold therapy (chrysotherapy). Mechanism of action is unknown but may relate to immunosuppressive effect on lymphocytes.

## **Indications and Clinical Uses**

Aurothioglucose (gold therapy) is used primarily for immune-mediated diseases. It has been used with some success to control immune-mediated skin diseases, such as pemphigus and immune-mediated arthritis. However, because of a lack of controlled trials to demonstrate efficacy and adverse effects that have been observed, the use in veterinary medicine has been uncommon.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects include dermatitis, nephrotoxicity, and blood dyscrasias.

#### **Contraindications and Precautions**

Do not use in animals with suppressed bone marrow or animals already receiving bone marrow-suppressing agents.

#### **Drug Interactions**

No drug interactions are reported in animals.

## **Instructions for Use**

Use of this drug has not been evaluated in veterinary medicine. No controlled clinical trials are available to determine efficacy in animals. This drug is often used in combination with other immunosuppressive drugs such as corticosteroids.

## **Patient Monitoring and Laboratory Tests**

Monitor patient's CBC periodically because gold salts have caused blood dyscrasias.

## **Formulations**

- Aurothioglucose has been discontinued and is no longer available. However, some forms still persist (e.g., from compounding pharmacies) in a 50-mg/mL injection.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. The stability of compounded formulations has not been evaluated.

## **Small Animal Dosage**

### **Dogs**

- Dogs <10 kg: 1 mg IM first week, 2 mg IM second week, 1 mg/kg/week maintenance. Dogs >10 kg: 5 mg IM first week, 10 mg IM second week, 1 mg/kg/week maintenance.

### **Cats**

- 0.5-1 mg/cat every 7 days IM.

## **Large Animal Dosage**

### **Horses**

- 1 mg/kg per week IM.

## **Regulatory Information**

Do not administer to animals intended for food.

## Azathioprine

ay-za-thye'oe-preen

**Trade and other names:** Imuran and generic

**Functional classification:** Immunosuppressive

### Pharmacology and Mechanism of Action

Thiopurine immunosuppressive drug. Acts to inhibit T-cell lymphocyte proliferation. It is active against T-cells and B-cells, thus producing immunosuppressive activity. The exact mechanism of action is not known. Azathioprine is initially spontaneously metabolized to 6-mercaptopurine (6-MP). The metabolite 6-MP is further metabolized via thiopurine methyltransferase (TPMT) to 6-methylmercaptopurine (6-MMP), which may be associated with adverse effects. It is also metabolized via TPMT to other metabolites, including 6-thioguanine (6-TG), which may be responsible for the immunosuppressive effects because it can accumulate in cells and acts as a purine antagonist that disrupts DNA in leukocytes. Other cells can use salvage pathways for purine synthesis, but stimulated lymphocytes are not capable of this synthesis.

### Indications and Clinical Uses

Azathioprine is used to treat various immune-mediated diseases in animals, including immune-mediated hemolytic anemia, pemphigus, and inflammatory bowel disease. It is often the first drug of choice, in addition to corticosteroids, for treatment of immune-mediated hemolytic anemia and pemphigus in dogs and is often used for inflammatory bowel disease. It is primarily used in dogs, and is not recommended in cats. There are some case reports for its successful use to treat immune-mediated disease in horses, but experience is limited. It is often administered with prednisone or prednisolone. Onset of action is delayed delayed for 4-6 weeks in some human patients. The onset of effects in animals has not been determined, but observations indicate that it occurs more quickly than in people.

### Precautionary Information

#### Adverse Reactions and Side Effects

Bone marrow suppression is the most serious concern. Additional adverse effects in dogs include diarrhea, increased risk of secondary infections, and vomiting. Hepatototoxicosis after administration of azathioprine also has been reported. Toxicity may be related to the metabolites, particularly 6-MMP. Individuals who have higher sensitivity to the suppressing effects of bone marrow should have dose reduced and high levels of this metabolite may be responsible for myelotoxicity and hepatotoxicity, although this has never been confirmed in dogs. The metabolite 6-TGN also can produce myelosuppression. There has been some association with development of pancreatitis when administered with corticosteroids. Sensitivity to the adverse effects, and prediction of therapeutic effects in people may be correlated with the levels of the metabolizing enzyme, thiopurine methyltransferase (TPMT). Some people are deficient and have a higher incidence of adverse effects. However, the TPMT levels in dogs are variable and have not been associated with either hepatotoxicity or myelotoxicity. Cats are deficient in TPMT and are particularly susceptible to toxicity.

#### Contraindications and Precautions

Exercise extreme caution and careful monitoring when administering to cats.

**Drug Interactions**

Administer with caution with other drugs that may suppress the bone marrow (e.g., cyclophosphamide and anticancer drugs). There is some evidence that concurrent use with corticosteroids may increase risk of pancreatitis. Do not administer with allopurinol because antagonism of xanthine oxidase may interfere with metabolism.

**Instructions for Use**

Azathioprine is usually used in combination with other immunosuppressive drugs (e.g., corticosteroids) to treat immune-mediated disease. Cats are very sensitive to the bone marrow-suppressing effects of azathioprine. Doses of 2.2 mg/kg to cats have produced toxicity, but some experts recommend starting cats with doses of 0.3 mg/kg/day. Alternatively, chlorambucil has been used instead of azathioprine in cats when immunosuppressive action is needed.

**Patient Monitoring and Laboratory Tests**

Monitor patient's CBC periodically because some animals are sensitive to the effects of azathioprine and its metabolite, 6-MP. After 2 weeks of treatment, a CBC is essential. Because of risk of hepatotoxicity, monitor hepatic enzymes and bilirubin regularly.

**Formulations**

Azathioprine is available in 25-, 50-, 75-, and 100-mg tablets and 10-mg/mL for injection.

**Stability and Storage**

Store in a tightly sealed container at room temperature. Compounded oral suspensions are stable for 60 days.

**Small Animal Dosage****Dogs**

- 2 mg/kg q24h PO initially, then 0.5-1 mg/kg q48h. In dogs, doses as high as 1.5 mg/kg q48h PO have been used with prednisolone.

**Cats (use cautiously)**

- Cats are sensitive to bone marrow-suppressing effects, and many clinicians avoid azathioprine in cats altogether. However, if administered to cats, one should start with 0.3 mg/kg q24h PO and adjust dose to q48h after careful monitoring. Tablet size may be as low as 1/30 to 1/50 of a tablet, which will require careful compounding.

**Large Animal Dosage****Horses**

- 3 mg/kg, PO, q24h.

**Regulatory Information**

Do not administer to animals intended for food.

**Azithromycin**

ay-zith-roe-my'sin

**Trade and other names:** Zithromax

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Azalide antibiotic. Similar mechanism of action as macrolides (e.g., erythromycin), which is to inhibit bacteria protein synthesis via inhibition of ribosome. Spectrum of activity is primarily gram-positive cocci, including streptococci and staphylococci. It also has good activity against *Mycoplasma* spp., *Chlamydia*, and some intracellular pathogens. The activity against *Toxoplasma* has been questionable. Pharmacokinetic data show extremely long plasma, tissue, and leukocyte half-lives in dogs, cats, and horses. It is minimally metabolized and very little active drug is excreted in the urine. Plasma half-life is 15-18 hours in horses, 35 hours in cats, and 30 hours in dogs. Volume of distribution also is large, with values exceeding 10 L/kg. Oral absorption in dogs is 90%, but less in cats (58%) and horses (40-45%). Azithromycin, like other long-acting macrolides, is characterized by low plasma drug concentrations, but much higher (100-200x) concentrations in leukocytes, bronchial secretions, and some tissues.

Azithromycin, like other macrolides, exert therapeutic benefits not solely explainable by antibacterial activity. Azithromycin has multiple immunomodulatory effects that likely contribute to the therapeutic response in respiratory infections, and perhaps other diseases. Even with infections caused by organisms not susceptible to azithromycin in vitro, such as infections caused by *Pseudomonas aeruginosa*, azithromycin has produced benefits by decreasing the virulence properties of the organism (e.g., inhibition of quorum sensing and inhibition of biofilm). Other beneficial effects may be caused by enhanced degranulation and apoptosis of neutrophils and inhibition of inflammatory cytokine production. It also may help clear infections by enhancing macrophage functions.

## Indications and Clinical Uses

Azithromycin is indicated for treatment of bacterial infections. It also has been used in people for a variety of respiratory infections in which the benefits are believed to be partially, if not predominantly, caused by the immunomodulatory properties. Antimicrobial spectrum is primarily gram positive. Azithromycin is not recommended for serious gram-negative infections. It may be used to treat infections caused by *Mycoplasma* and other atypical organisms. Azithromycin has been used to treat intracellular organisms because of its ability to concentrate in leukocytes. One of the uses has been to treat infections caused by *Rhodococcus equi* in foals. However, in one comparative study, clarithromycin plus rifampin had better clinical success in foals than azithromycin plus rifampin. In foals, azithromycin, administered at a dose of 10 mg/kg q48h oral during the first 2 weeks after birth, has been used prophylactically to decrease *Rhodococcus* infection in foals at high risk (farms with high endemic risk). In horses, azithromycin also has been used to treat proliferative enteritis caused by *Lawsonia intracellularis*. Azithromycin has been used in cats to treat upper respiratory infections. There are no controlled clinical trials to document success for this use; however, this treatment has been common among veterinarians. Azithromycin administered to cats with infections caused by *Chlamydophila felis* (formerly *Chlamydia psittaci*), at 10-15 mg/kg once daily for 3 days and thereafter two times per week, was not effective for eliminating the organism, although clinical signs improved (perhaps via the immunomodulatory effects). However, azithromycin was not effective in cats for treatment of *Mycoplasma hemofelis* (hemobartonellosis). When azithromycin was administered to dogs with pyoderma at a dose of either 10 mg/kg on day 1 followed by 5 mg/kg on days 2 through 5 or 5 mg/kg given 2 days per week for 3 weeks, the response was equal statistically to cephalexin at 22 mg/kg twice daily. In dairy calves, azithromycin administration significantly suppressed shedding of *Cryptosporidium parvum* and improved clinical signs. However,

in cattle and pigs, other long-acting macrolides approved for those species are recommended over azithromycin.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects to azithromycin have not been reported in publications. However, vomiting is likely with high doses. Diarrhea may occur in some patients. Changes in the consistency of the feces and diarrhea have been reported in horses that were administered recommended doses. The long-term safety in adult horses is not known. Azithromycin has a history of a favorable safety profile after many years of use in people. A warning occurs on the human label warning of potentially serious cardiac arrhythmias from azithromycin use, but these problems have not been observed in animals.

#### **Contraindications and Precautions**

Use cautiously in animals with a history of vomiting. Administration to adult horses has been associated with diarrhea. Do not administer IV solution as a bolus or IM.

#### **Drug Interactions**

Drug interactions have not been reported in animals. This class of drugs has the potential to inhibit some cytochrome P450 enzymes that are involved in drug metabolism, but azithromycin is less likely than erythromycin or clarithromycin to interfere with cytochrome P450 enzymes.

### **Instructions for Use**

Azithromycin may be better tolerated than erythromycin. A primary difference from other antibiotics is the high intracellular concentrations achieved and long half-life that allows for intermittent administration. Although azithromycin has been commonly used for infections in dogs and cats, there is insufficient clinical trial evidence for many uses. Doses listed in the dosage section are based primarily on anecdotal accounts and clinical experience rather than efficacy studies. To prepare IV solution, add 4.8 mL sterile water to each 500-mg vial and shake. Further dilute this solution with either 500 or 250 mL diluent to a solution of 1 or 2 mg/mL. When administered IV, a 1-mg/mL solution should be administered over a 3-hour period or 2 mg/mL should be administered over 1 hour.

### **Patient Monitoring and Laboratory Tests**

Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 2$  mcg/mL.

### **Formulations**

- Azithromycin is available in 250-, 500- and 600-mg tablets, 100- and 200-mg/5 mL oral suspension, and 500-mg vials for injection. Also, 1-g packets are available for mixing with water.

### **Stability and Storage**

Stable if maintained in manufacturer's original formulation. Stability has not been reported for compounded formulations. IV solution is stable after reconstitution for 48 hours at room temperature.

## Small Animal Dosage

### Dogs

- A range of doses has been used, starting with 10 mg/kg once daily, PO, for 5-7 days, then decreasing to every other day. Alternatively, 5 mg/kg per day has been used by some veterinarians, either once per day or once every other day.

### Cats

- 5-10 mg/kg, once daily for 7 days, PO, followed by administration q48h; or 10-15 mg/kg daily for 3 days, followed by the same dose twice weekly, PO.
- Upper respiratory infection: 15 mg/kg, initially for the first 3 days, then q72h, PO.

## Large Animal Dosage

### Horses

- For *Rhodococcus equi*: 10 mg/kg q24h, PO initially for 5 days, then q48h after a response is seen.
- Foals: 10 mg/kg q48h, PO. For foals, the 1-g packet can be mixed with water to create suspension for oral administration.
- Adult horses: 10 mg/kg PO, q48h.

### Cattle

- 10 mg/kg IM.

### Calves

- For cryptosporidiosis: 33 mg/kg once daily for 7 days, PO.

## Regulatory Information

Withdrawal times have not been established for animals producing food, but when administered to cattle, it persisted in milk with a half-life of approximately 160 hours and persisted longer in mastitic milk than in normal milk.



## Benazepril Hydrochloride

ben-ay'zeh-pril hye-droe-klor'ide

**Trade and other names:** Lotensin (human preparation) and Fortekor, Benazecare (veterinary preparation)

**Functional classification:** Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

### Pharmacology and Mechanism of Action

Angiotensin-converting enzyme (ACE) inhibitor. Inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and will also stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The inhibition of aldosterone will decrease sodium and water retention. Benazepril, like other ACE inhibitors, will produce vasodilation and decrease aldosterone-induced congestion. Angiotensin-converting enzyme inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins. Unlike enalapril, benazepril has a dual mode of elimination through the kidneys and liver and clearance is not affected in animals with kidney disease. Duration of ACE-inhibiting action is 16-24 hours, despite a short plasma half-life, because of high-affinity binding to ACE.

### Indications and Clinical Uses

Benazepril, like other ACE inhibitors, is used to treat hypertension and congestive heart failure (CHF). Evidence shows that it may decrease the likelihood of developing cardiomyopathy in some dogs, but other studies failed to show this benefit. For treatment of occult mitral valve disease in dogs, there has not been a benefit of therapy. It may benefit some cats in heart failure or with systemic hypertension; however, some cats with hypertension may not respond, and ACE inhibitors are not considered a primary treatment for hypertension in cats. Benazepril has limited antihypertensive effects in cats with naturally occurring kidney disease, but may be effective in slowing the progression of renal failure. In studies in which it has been used in cats with renal insufficiency, it was associated with a small reduction in systemic hypertension, reduced glomerular filtration pressure, decreased glomerular hypertension, reduction in urine protein loss, and an increase in glomerular filtration rate (GFR), but no overall benefits on survival. In dogs, it produces similar benefits to animals with kidney disease (decreased proteinuria, increased GFR, and lower blood pressure), but it does not increase survival. Nevertheless, many renal experts recommend including an ACE-inhibitor (benazepril or enalapril) in the initial treatment for dogs with proteinuria caused by glomerular disease.

### Precautionary Information

#### Adverse Reactions and Side Effects

Benazepril has been well tolerated in dogs and cats with chronic renal failure. However, it may cause azotemia in some patients; carefully monitor renal parameters after initiation of treatment, particularly in patients receiving high doses of diuretics.

#### Contraindications and Precautions

Discontinue ACE inhibitors in pregnant animals. Angiotensin-converting enzyme inhibitors cross the placenta and have caused fetal malformations and death of the fetus.

#### Drug Interactions

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease vasodilating effects. Benazepril, like other ACE-inhibitors, may be used with other cardiovascular drugs and

furosemide. However, it will not prevent increases in aldosterone (caused by activation of RAAS) in patients treated with furosemide.

### Instructions for Use

Dose is based on approved use in dogs in Europe and Canada. Monitor renal function and electrolytes 3-7 days after initiating therapy and periodically thereafter. In studies in cats, there was no benefit to doses higher than 0.5-1 mg/kg/day.

### Patient Monitoring and Laboratory Tests

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

### Formulations

- Benazepril is available in 5-, 10-, 20-, and 40-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 0.25-0.5 mg/kg q12-24h PO (0.5 mg/kg q24h in most patients). Increase by 0.5 mg/kg if needed, to maximum of 2 mg/kg q24h.

#### Cats

- Systemic hypertension and renal disease: 0.5-1 mg/kg/day q24h PO. Alternative dose for cats is 2.5 mg per cat per day, for cats up to 5 kg body weight, PO.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Do not administer to animals intended for food.

Racing Commissioners International (RCI) Classification: 3

## Betamethasone

bay-tah-meth'ah-sone

**Trade and other names:** Celestone, betamethasone acetate, and betamethasone benzoate

**Functional classification:** Corticosteroid

### Pharmacology and Mechanism of Action

Potent, long-acting corticosteroid. Anti-inflammatory and immunosuppressive effects are approximately 30 times more than cortisol. Anti-inflammatory effects are complex but primarily occur via inhibition of inflammatory cells and suppression of expression of inflammatory mediators.

### Indications and Clinical Uses

Betamethasone is used for treatment of inflammatory and immune-mediated disease. It is used for similar indications as prednisolone and dexamethasone.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic-pituitary-adrenal (HPA) axis suppression. Adverse effects include gastrointestinal (GI) ulceration, hepatopathy, increased risk of diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include Demodex, toxoplasmosis, fungal infections, and urinary tract infections (UTIs). In horses, additional adverse effects may include risk of laminitis.

### Contraindications and Precautions

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously in diabetic animals, animals with renal failure, or pregnant animals.

### Drug Interactions

No drug interactions are reported in animals. However co-administration with other drugs may increase risk of adverse effects. For example, administration with nonsteroidal anti-inflammatory drugs (NSAIDs) may increase the risk of gastrointestinal problems.

## Instructions for Use

Betamethasone is used for similar indications as dexamethasone because of similar potency and duration of effect. Topical forms of betamethasone also are available.

## Patient Monitoring and Laboratory Tests

Monitor complete blood count (CBC) and plasma cortisol.

## Formulations

- Betamethasone is available in 600-mcg (0.6-mg) tablets and 3 mg/mL sodium phosphate injection. (Tablets may be discontinued from some distributors.)

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- Anti-inflammatory effects: 0.1-0.2 mg/kg q12-24h PO.
- Immunosuppressive effects: 0.2-0.5 mg/kg q12-24h PO.

## Large Animal Dosage

- 0.05-0.1 mg/kg q24h IM or PO.

## Regulatory Information

No withdrawal times are established for animals intended for food (extralabel use).  
RCI Classification: 4

## Bethanechol Chloride

beh-than'eh-kole klor'ide

**Trade and other names:** Urecholine

**Functional classification:** Cholinergic

## Pharmacology and Mechanism of Action

Muscarinic, cholinergic agonist. Parasympathomimetic. Bethanechol stimulates gastric and intestinal motility. It also stimulates contraction of the urinary bladder via muscarinic receptor activation. Bethanechol, like other carbamoyl esters, resists hydrolysis by acetylcholinesterase to produce a more sustained response. The onset of action is usually 10 minutes after injection and 30-60 minutes after oral administration. Duration of effect is 4-6 hours.

## Indications and Clinical Uses

Bethanechol is used in small animals to increase contraction of the urinary bladder. In large animals, it may increase gastrointestinal motility, but the efficacy for treating gastrointestinal stasis problems is questionable.

### Precautionary Information

#### Adverse Reactions and Side Effects

High doses of cholinergic agonists will increase motility of the GI tract and cause abdominal discomfort and diarrhea. Bethanechol can cause circulatory depression in sensitive animals.

#### Contraindications and Precautions

Do not use in patients with suspected gastrointestinal or urinary obstruction.

#### Drug Interactions

Anticholinergic drugs (atropine, scopolamine, etc.) will antagonize the effects of bethanechol.

## Instructions for Use

Administer injection SQ only. Doses are derived from extrapolation of human doses or via empiricism. There are no well-controlled efficacy studies available for veterinary species.

Bethanechol is no longer available from commercial sources, but some veterinary compounding pharmacists may be able to supply veterinarians.

## Patient Monitoring and Laboratory Tests

Monitor GI function.

## Formulations

- Bethanechol is available in 5-, 10-, 25-, and 50-mg tablets and 5-mg/mL injection. (Commercial preparations are no longer available, but are available through some compounding pharmacies.)

## Stability and Storage

Store in a tightly sealed container at room temperature. Compounded oral suspensions prepared from tablets are not stable.

## Small Animal Dosage

### Dogs

- 5-15 mg/dog q8h PO (2.5 mg per dog for small dogs).

### Cats

- 1.25-5 mg/cat q8h PO.

## Large Animal Dosage

### Horses

- 0.025 mg/kg SQ, once.

### Cattle

- 0.07 mg/kg SQ, once.

**Regulatory Information**

No withdrawal times are established for animals intended for food (extralabel use). However, the Food Animal Residue Avoidance Databank (FARAD) (1-888-873-2723) recommends a 21-day withdrawal time for slaughter.

RCI Classification: 4

**Bisacodyl**

biss-ah-koe'dil

**Trade and other names:** Dulcolax

**Functional classification:** Laxative

**Pharmacology and Mechanism of Action**

Laxative/cathartic. Bisacodyl acts via local stimulation of GI motility, most likely by irritation of the bowel.

**Indications and Clinical Uses**

Bisacodyl is used as a laxative or for procedures in which bowel evacuation is necessary. It may be used with polyethylene glycol electrolyte solution (e.g., GoLYTELY) to cleanse the bowel prior to endoscopy or surgical procedures.

**Precautionary Information****Adverse Reactions and Side Effects**

Abdominal discomfort. Fluid and electrolyte loss. Avoid chronic use.

**Contraindications and Precautions**

Avoid use in patients with renal disease. Avoid overuse.

**Drug Interactions**

No drug interactions are reported in animals.

**Instructions for Use**

Bisacodyl is available as an over-the-counter (OTC) tablet. Doses are derived from extrapolation of human doses or via empiricism. There are no well-controlled efficacy studies available for veterinary species. Onset of action is approximately 1 hour after administration.

**Patient Monitoring and Laboratory Tests**

Monitor electrolytes in animals if used chronically.

**Formulations**

- Bisacodyl is available in 5-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs and Cats**

- 5 mg/animal q8-24h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

## Bismuth Subsalicylate

biz'muth sub-sal-iss'ih-late

**Trade and other names:** Pepto-Bismol

**Functional classification:** Antidiarrheal

## Pharmacology and Mechanism of Action

Antidiarrheal agent and GI protectant. Precise mechanism of action is unknown, but antiprostaglandin action of salicylate component may be beneficial for enteritis. The bismuth component is efficacious for treating infections caused by spirochete bacteria (*Helicobacter pylori* gastritis). Bismuth subsalicylate in Pepto-Bismol contains five sources of salicylate, which are absorbed systemically after oral administration. Bismuth subsalicylate also may be found in other antidiarrhea preparations, such as kaolin-pectin formulations (e.g., Kaopectate).

## Indications and Clinical Uses

Bismuth subsalicylate is used for symptomatic treatment of diarrhea in small and large animals. Efficacy has not been established for animals. However, in people it has been shown effective for treating or preventing diarrhea caused by enterotoxigenic *Escherichia coli* (ETEC).

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are uncommon. Owners should be warned that bismuth will discolor stools black.

### Contraindications and Precautions

The salicylate component is absorbed systemically, and overuse should be avoided in animals that cannot tolerate salicylates, such as cats and animals allergic to aspirin.

### Drug Interactions

No drug interactions are reported in animals. However, it may possibly exacerbate effects of other NSAIDs administered to animals. The bismuth component may prevent oral absorption of some drugs.

## Instructions for Use

Bismuth subsalicylate is available as an OTC product. Doses are derived from extrapolation of human doses or via empiricism. There are no well-controlled efficacy studies available for veterinary species.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

**Formulations**

- Bismuth subsalicylate is available in oral suspension in 262 mg/15 mL or 525 mg/mL in extra-strength formulation and 262-mg tablets. Two tablespoons (30 mL) contain 270-mg salicylate.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs and Cats**

- 1-3 mL/kg/day (in divided doses) PO.

**Large Animal Dosage****Calves**

- 30 mL per calf, q30min for 8 doses PO.

**Horses**

- 1-2 mL/kg q6-8h PO.

**Regulatory Information**

No withdrawal times are established for animals intended for food (extralabel use). Because the salicylate component may be systemically absorbed, withdrawal times should be considered for the salicylate component (similar to aspirin).

**Bisoprolol Fumarate**

bis-oh'-proe-lol

**Trade and other names:** Zebeta

**Functional classification:** Antiarrhythmic, beta blocker

**Pharmacology and Mechanism of Action**

Bisoprolol is a synthetic beta<sub>1</sub>-selective beta-adrenergic receptor blocker with a low affinity for beta<sub>2</sub>-receptors in bronchial smooth muscle, blood vessels, and fat cells and no intrinsic sympathomimetic activity. Typical cardioselective effects include lower heart rate, decreased cardiac output, and inhibition of renin release by kidneys. At higher doses it will lose beta<sub>1</sub> selectivity and inhibit some beta<sub>2</sub> receptors to affect bronchial and vascular smooth muscle. Clearance in dogs is balanced (60% metabolized by the liver and 40% excreted unchanged), distinguishing bisoprolol from lipophilic beta blockers such as carvedilol and metoprolol and from hydrophilic beta blockers like atenolol. In dogs, bisoprolol has high and consistent oral absorption (91%) and a half-life of 4 hours. Although bisoprolol prolongs survival in human patients with heart failure, similar studies have not been conducted in dogs or cats.

**Indications and Clinical Uses**

Bisoprolol is a beta<sub>1</sub> blocker that is somewhat cardioselective and therefore is indicated for conditions that require a reduction in heart rate, heart conductivity, or contractility. Such conditions include tachyarrhythmias and atrial fibrillation. In people it is used to treat hypertension, but this use has not been explored in animals.

## Precautionary Information

### Adverse Reactions and Side Effects

Beta blockade will result in adverse effects that are attributed to decreased adrenergic tone in the heart. Bradycardia and heart block are possible. At high doses or in sensitive doses, bisoprolol may produce bronchospasm. Treat bradycardia from overdose with atropine.

### Contraindications and Precautions

Use cautiously in animals with airway disease, myocardial failure, and cardiac conduction disturbances. Use cautiously in animals with low cardiac reserve.

### Drug Interactions

Use cautiously with other drugs that may decrease cardiac contraction or heart rate. Concurrent use of rifampin may increase the metabolic clearance of bisoprolol.

## Instructions for Use

Dosing precautions are similar to other beta-blocking drugs.

## Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm. Monitor blood pressure in patients prone to hypotension.

## Formulations

- Bisoprolol is available in 5- and 10-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 0.1-0.2 mg/kg q8-12h, PO.

### Cats

- No dose has been established for cats.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Bleomycin Sulfate

blee-oh-mye'sin sul'fate

**Trade and other names:** Blenoxane

**Functional classification:** Anticancer agent

## Pharmacology and Mechanism of Action

Anticancer antibiotic agent. Exact mechanism of action is unknown, but it may bind to DNA and prevent synthesis.

## Indications and Clinical Uses

Bleomycin is used for treatment of various sarcomas and carcinomas.



**Precautionary Information****Adverse Reactions and Side Effects**

Bleomycin causes local reaction at site of injection, pulmonary toxicity, fever, and chills in people. Side effects are not well documented in veterinary species.

**Contraindications and Precautions**

Do not use in animals with suppressed bone marrow.

**Drug Interactions**

No drug interactions are reported in animals.

**Instructions for Use**

Injectable solution usually used in combination with other anticancer agents. Consult anticancer protocols for details regarding use.

**Patient Monitoring and Laboratory Tests**

Monitor CBC during treatment.

**Formulations**

- Bleomycin is available in 15- and 30-unit vials for injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Refrigerate vials after opening. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- 10 units/m<sup>2</sup> IV or SQ for 3 days, then 10 units/m<sup>2</sup> weekly. (Maximum cumulative dose 200 units/m<sup>2</sup>.)

**Cats**

- No dose is available for cats.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. Because it is an anticancer agent, do not administer to food-producing animals.

**Boldenone Undecylenate**

bole'de-none un-de-sil-en'ate

**Trade and other names:** Equipoise

**Functional classification:** Hormone, anabolic agent

**Pharmacology and Mechanism of Action**

Anabolic steroid. Boldenone is a steroid ester designed to maximize anabolic effects while minimizing androgenic action (see also "Methyltestosterone"). Anabolic agents have been used for reversing catabolic conditions, increasing weight gain, increasing

muscling in animals, and stimulating erythropoiesis. Stanozolol is a similar drug used in horses. There are no documented differences in efficacy among the anabolic steroids.

### Indications and Clinical Uses

Boldenone is an anabolic agent. It is used primarily in horses to improve nitrogen balance, reduce overexertion associated with exercise, and improve training. It may also improve appetite and improve weight gain when used with a well-balanced diet. Boldenone is a long-lasting agent, and effects may persist for 6 weeks after an intramuscular injection.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects from anabolic steroids can be attributed to the androgenic action of these steroids. Increased masculine effects are common. Increased aggressiveness may be observed. Increased incidence of some tumors has been reported in people, and 17 alpha-methylated oral anabolic steroids (oxymetholone, stanozolol, and oxandrolone) are associated with hepatic toxicity.

#### Contraindications and Precautions

This drug is abused by humans to enhance athletic performance and is a controlled substance. Do not administer to animals intended for food. Do not administer to pregnant animals.

#### Drug Interactions

There are no significant drug interactions known; however, use cautiously with other drugs that may affect liver function.

### Instructions for Use

For many indications, use in animals is based on experience in people or anecdotal experience in animals.

### Patient Monitoring and Laboratory Tests

Monitor liver enzymes for signs of hepatic injury (cholestatic) during treatment.

### Formulations

- Boldenone is available in 25- and 50-mg/mL injection in sesame oil.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze. Do not mix with aqueous solutions.

### Small Animal Dosage

- Doses have not been reported for small animals.

### Large Animal Dosage

#### Horses

- 1.1 mg/kg IM. Injection may be repeated every 3 weeks.

### Regulatory Information

Do not administer to animals intended for food.

Schedule III controlled drug.

RCI Classification: 4

## Bromide

broe'mide

**Trade and other names:** Potassium bromide and sodium bromide

**Functional classification:** Anticonvulsant

### Pharmacology and Mechanism of Action

Anticonvulsant. Exact mechanism of action is uncertain. Anticonvulsant action is to stabilize neuronal cell membranes. Bromide is a halide salt and may affect neuronal chloride ion channels, causing hyperpolarization of neuronal membranes and raising the seizure threshold. By changing the chloride conductance in neuronal membranes, it may stabilize epileptic foci in the brain. In dogs, oral absorption is 46%. It is not metabolized, and most is eliminated by the kidneys. The half-life is long—11 days in cats, and it has ranged from 25 days to 46 days in dogs. Bromide is available in two forms: sodium bromide (78% bromide) and potassium bromide (67% bromide).

The use of potassium bromide for seizure control dates back to the 1850s in humans. But in the 20<sup>th</sup> century, the use of bromide for treating seizure disorders in people diminished because of common adverse effects and availability of other medications.

### Indications and Clinical Uses

Bromide ordinarily is used in patients with seizure disorders that have been refractory to phenobarbital. Usually, patients are treated with both phenobarbital and bromide. However, some patients have been treated with bromide as a single therapy for epilepsy. If bromide is added to phenobarbital therapy, it allows for a reduction in phenobarbital dose (reduce by 25% every 6 weeks). Bromide has not been as effective for treating cats with seizure disorders as in dogs. Cats have more adverse effects and are less well controlled; therefore, bromide is rarely recommended for a treatment in cats.

### Precautionary Information

#### Adverse Reactions and Side Effects

Common side effects include polyuria/polydipsia (PU/PD), polyphagia, ataxia, sedation, and gastrointestinal upset. More serious adverse effects are related to high levels of bromide (bromism) and are more specific for the central nervous system (CNS). Signs of toxicosis are CNS depression, delirium, hyperexcitability, weakness, and ataxia. Hind limb stiffness and abnormal gait also may be signs of bromide toxicosis. If adverse effects occur, discontinuation of the medication usually results in resolution of the clinical signs in several days. Resolution may be faster (within hours) with aggressive saline diuresis.

Nausea and pancreatitis have been reported in dogs, and there is evidence that a combination of bromide and phenobarbital in dogs may increase the risk of pancreatitis. However, there is no direct evidence that bromide alone produces pancreatic toxicity. There is no evidence available to indicate that bromide treatment affects thyroid function in dogs.

Some dogs show paradoxical excitement with bromide treatment. In many cats, bronchitis resembling allergic airway disease has been observed. In cats this may be characterized by coughing.

#### Contraindications and Precautions

Consider using sodium bromide, rather than potassium bromide, in patients with hypoadrenocorticism or in any patients in which potassium regulation is a

problem. Likewise, consider the sodium content of administration in animals with congestive heart failure or hypertension. Diets high in chloride will cause a shorter half-life and need for a higher dose. Monitor plasma concentrations and adjust dose as necessary whenever changing diets, because increasing chloride in the diet will shorten the half-life and vice versa. If the diet is high in chloride (Hill's h/d, s/d, I/d, and others), higher starting doses may be necessary. Administration of bromide will interfere with some blood chemistry analysis (e.g., false elevation of chloride).

### Drug Interactions

Diets high in chloride will cause a shorter half-life and need for a higher dose. Administration of bromide will interfere with some blood chemistry analysis (e.g., false elevation of chloride).

### Instructions for Use

Bromide usually is administered in combination with phenobarbital. Sodium bromide can be substituted for potassium bromide. When considering doses for sodium bromide, slight dose adjustments should be considered. Potassium bromide is 67% bromide, and sodium bromide is 78% bromide. The dose of sodium bromide should be approximately 15% less (e.g., 30 mg/kg of potassium bromide is equivalent to 25 mg/kg of sodium bromide).

### Patient Monitoring and Laboratory Tests

Monitor serum bromide concentrations to adjust dose. Effective plasma concentrations should be 1-2 mg/mL (100-200 mg/dL), but if used alone (without phenobarbital), higher concentrations of 2-2.5 mg/mL (200-250 mg/dL) and as high as 4 mg/mL may be needed. Most veterinary laboratories can perform a test for bromide in plasma or serum.

### Formulations

- Bromide is usually prepared as an oral solution. Although there are no commercial forms approved by the U.S. Food and Drug Administration (FDA), compounding pharmacists can prepare a solution. To prepare the oral solution, mix 25 g of potassium bromide with 60 mL of purified water, then add a sufficient quantity of corn syrup to make 100 mL. This formulation will result in a bromide concentration of approximately 151-185 mg/mL. This solution is stable for 180 days. For sodium bromide oral solution, mix 21.6 g sodium bromide with 60 mL purified water, then add a sufficient quantity of corn syrup to make 100 mL. This formulation will result in a concentration of approximately 151-185 mg/mL. This solution is stable for 180 days.
- A pharmacist should prepare the intravenous solution in sterile water and filter it to remove impurities. To prepare injectable solution, add 3 g of sodium bromide with a sufficient quantity of sterile water to make 100 mL. This formulation will result in a bromide concentration of approximately 21-25.6 mg/mL. It is stable for 180 days and should be stored in the refrigerator to decrease the risk of microbial growth.

### Stability and Storage

Store in a tightly sealed container. Compounded formulations in aqueous solutions are stable for at least 180 days. Refrigerate injectable solution to prevent bacterial growth. Do not mix with salt-containing flavorants or solutions.

## 82 Bromocriptine Mesylate

### Small Animal Dosage

#### Cats

- 30 mg/kg q24h PO.

#### Dogs

- 30-40 mg/kg q24h PO. If administered without phenobarbital, higher doses of up to 40-50 mg/kg may be needed. If animals are on diets high in chloride, higher doses may be needed. Adjust doses by monitoring plasma concentrations.
- Oral loading dose: 600 mg/kg divided over 3-5 days (200 mg/kg once a day for 5 days also has been used), PO. Alternatively, 60 mg/kg/day has been administered for 15 days to achieve a plasma concentration of 100 mg/dL, and 200 mg/dL by 60 days.
- IV loading dose for sodium bromide: 800 to 1200 mg/kg infused over 8 hours (it is critical to use sodium bromide instead of potassium bromide for this use).

### Large Animal Dosage

#### Horses

- 100 mg/kg loading dose, followed by 25 mg/kg q24h, PO.
- No dose has been reported for other large animals.

### Regulatory Information

Do not administer to animals intended for food.

## Bromocriptine Mesylate

broe-moe-krip'teen mess'ih-late

**Trade and other names:** Parlodel

**Functional classification:** Dopamine agonist

### Pharmacology and Mechanism of Action

Dopaminergic agonist. Antiprolactin agent. Bromocriptine is a lactation inhibitor. It reduces serum prolactin concentration by inhibition of release from the anterior pituitary gland by binding to dopamine ( $D_2$ ) receptors in the CNS. The binding of  $D_2$  receptors restores hormonal function in the pituitary. Through the action on the dopamine pituitary receptors, bromocriptine may decrease corticotropin (adrenocorticotrophic hormone [ACTH]) release and has been used in animals (especially horses) for treating pituitary-dependent hyperadrenocorticism (PDH). It has not been effective for treating canine PDH (Cushing syndrome). It also stimulates postsynaptic dopamine receptors and has been used to treat dopamine-deficient neurodegenerative diseases.

### Indications and Clinical Uses

In people, bromocriptine is used for its antiparkinson effect and to inhibit lactation associated with excess prolactin. It also has been used to treat acromegaly. Bromocriptine has been used to treat disorders associated with dopamine deficiency in animals. In dogs, bromocriptine has been used to terminate pregnancy when used in combination with a prostaglandin (dinoprost or cloprostenol). In this combination, it was 100% effective for terminating pregnancy in dogs. In horses, bromocriptine may decrease ACTH release and has been used in treating equine pituitary pars intermedia dysfunction (Cushing syndrome), but pergolide is usually a preferred treatment.

## Precautionary Information

### Adverse Reactions and Side Effects

Pyometra may occur in dogs after it has been used to induce abortion. Bromocriptine may cause mammary gland enlargement. When terminating pregnancy, bromocriptine is used in combination with prostaglandin F<sub>2</sub>alpha. Adverse effects (vomiting, nausea, and retching) may occur as a result of the prostaglandin. Bromocriptine will inhibit lactation.

### Contraindications and Precautions

Except when used for termination of pregnancy, do not use in pregnant animals. Do not use in nursing animals. Women handling bromocriptine should use caution to avoid exposure.

### Drug Interactions

No drug interactions have been reported in animals. However, it will exacerbate the effects of selegiline. Do not administer with monoamine oxidase inhibitors (MAOIs).

## Instructions for Use

Use of bromocriptine is limited to treatment of some endocrine disorders. Studies of efficacy are limited. Bromocriptine has been used to terminate pregnancy in dogs in combination with prostaglandin F<sub>2</sub>alpha. For this use, administer 15 mcg/kg q12h PO on day 1, 20 mcg/kg 12h PO on days 2 and 3, and 30 mcg/kg q12h PO thereafter for an average of 4-5 days. Ten days may be needed in some dogs. A prostaglandin (cloprostenol sodium) should be used at a dose of 1 mcg/kg q48h SQ during this regimen.

## Patient Monitoring and Laboratory Tests

Monitor pregnant animals carefully, especially if bromocriptine has been used to terminate pregnancy.

## Formulations

- Bromocriptine is available in 5-mg capsules and 2.5-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- Termination of pregnancy: 15 mcg/kg q12h PO on day 1, 20 mcg/kg 12h PO on days 2 and 3, and 30 mcg/kg q12h PO thereafter for an average of 4-5 days. For treatment success, it should be administered in combination with prostaglandin F<sub>2</sub>alpha.
- Other conditions: 0.02-0.04 mg/kg q12h PO.

### Cats

- 0.02-0.04 mg/kg q12h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

## Budesonide

byoo-dess'oh-nide

**Trade and other names:** Entocort

**Functional classification:** Anti-inflammatory, corticosteroid

### Pharmacology and Mechanism of Action

Budesonide is a locally acting corticosteroid, but is 1000 times more active than prednisolone as a corticosteroid. It is approved for use in people, but there has been only limited use in small animals. Budesonide granules are contained in an ethylcellulose matrix that is coated with methacrylic acid polymer. This coating does not release the drug until the pH is  $>5.5$ . Therefore, the drug is not usually released until it reaches the distal GI tract. Once released, it accumulates in intestinal cells and is stored by esterification with fatty acids. If any is absorbed, 80%-90% is inactivated by metabolism first-pass effects. Therefore, it has primarily a local effect on the intestine, and systemic glucocorticoid effects are minimized. In humans it has been as effective as other drugs for treatment of Crohn disease.

### Indications and Clinical Uses

In animals it has been used to treat inflammatory bowel disease. The most common use has been for treating colitis in dogs or inflammatory bowel disease in cats. It has been safe and effective for treating inflammatory bowel disease in dogs, however may produce some side effects that are similar to prednisone. Other reports of successful treatment are mostly anecdotal.

### Precautionary Information

#### Adverse Reactions and Side Effects

There is some systemic absorption, as evidenced by decreased response to ACTH and decreased cortisol after 30-day treatment to dogs at 3 mg/m<sup>2</sup>, but other side effects were not observed and other variables were not affected. Some mild elevation of liver enzymes may occur in dogs.

#### Contraindications and Precautions

No known contraindications. However, some of the drug may be absorbed systemically; therefore use with caution in animals that should not receive corticosteroids.

#### Drug Interactions

Do not administer with drugs that increase stomach pH (antacids, antisecretory drugs). Because budesonide is metabolized by cytochrome P450 enzymes, other drugs that inhibit these enzymes (see Appendix I) may inhibit metabolism.

### Instructions for Use

Use in animals has been limited to anecdotal experience and small clinical studies. The capsules should not be crushed or compounded for animals, unless action in the proximal portion of the intestine is desired.

### Patient Monitoring and Laboratory Tests

Monitor corticosteroid effects and, preferably, conduct an ACTH-stimulation test to determine degree of adrenal suppression with chronic use. Some elevations in liver enzymes may occur in dogs.

### Formulations

- Budesonide is available in 3-mg capsules.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not crush capsules.

### Small Animal Dosage

#### Dogs and Cats

- 0.125 mg/kg q8-12h PO. Dose interval may be increased to every 24 hours when condition improves.
- In dogs, intact 3-mg capsules, once per day, have been administered; but in cats, doses of 0.5 to 0.75 mg per cat per day are administered by reformulating capsules.
- Full range of doses for dogs: 3-7 kg, 1 mg every 24 hours; 7-15 kg, 2 mg every 24 hours; 15-30 kg, 3 mg every 24 hours; > 30 kg, 5 mg every 24 hours.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No regulatory information is available. Because of minimal systemic absorption expected, no withdrawal time is suggested.

RCI Classification: 4

## Bunamidine Hydrochloride

byoo-nam'ih-deen hye-droe-klor'ide

**Trade and other names:** Scolaban

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Bunamidine hydrochloride damages the integrity of protective integument on cestode parasites. It is effective against various species of tapeworms in animals.

### Indications and Clinical Uses

Bunamidine is used as an anticestodal agent to treat tapeworm infections in dogs and cats.

#### Precautionary Information

##### Adverse Reactions and Side Effects

Vomiting and diarrhea have occurred after use.

##### Contraindications and Precautions

Avoid use in young animals.

##### Drug Interactions

No drug interactions are reported in animals.

### Instructions for Use

Do not break tablets. Administer tablets on empty stomach. Do not feed animal for 3 hours after administration.



## 86 Bupivacaine Hydrochloride

### Patient Monitoring and Laboratory Tests

Monitor fecal samples for evidence of parasites.

### Formulations

- Bunamidine is available in 400-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 20-50 mg/kg once PO.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Bupivacaine Hydrochloride

byoo-piv'ah-kane hye-droe-klor'ide

**Trade and other names:** Marcaine, Exparel, and generic brands

**Functional classification:** Local anesthetic

### Pharmacology and Mechanism of Action

Local anesthetic. Bupivacaine inhibits nerve conduction via sodium channel blockade. Bupivacaine has a slow onset of action (20 minutes), but is longer acting (6-8 hours) and more potent than lidocaine or other local anesthetics. Epidural onset of action is approximately 15-20 minutes with a duration of 2-4 hours.

### Indications and Clinical Uses

Bupivacaine is used for local anesthesia and epidural analgesia/anesthesia. It is administered by local infiltration or by epidural injection. There is also a liposomal injection as a suspension in multivesicular liposomes (Exparel) contained in a delivery system (DepoFoam drug delivery system). After injection of Exparel into soft tissue, bupivacaine is released from the multivesicular liposomes over a period of time (96 hours). This formulation is used to infiltrate around a surgical site for a local anesthetic effect.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are rare with local infiltration. High doses absorbed systemically can cause nervous system signs (tremors and convulsions). The toxic dose in cats is 5 mg/kg. In cats, signs of toxicity include bradycardia, arrhythmias, tremors, muscle twitching, and seizures. After epidural administration, respiratory paralysis is possible with high doses.

**Contraindications and Precautions**

When using for epidural anesthesia, respiratory support should be available. Some formulations contain epinephrine (1:200,000) and should not be administered to animals that are prone to reactions from epinephrine.

**Drug Interactions**

No drug interactions are reported in animals.

**Instructions for Use**

Used for local infiltration or infusion into epidural space. For epidural injection, the volume of injection is approximately 0.2 mL/kg, or not to exceed 6 mL for large dogs. Ordinarily, the dose for a nerve block in small animals does not exceed 1 mg/kg. One may mix 0.1 mEq sodium bicarbonate per 10-mL solution to increase pH, decrease pain from injection, and produce a shorter onset of action. Use immediately after mixing with bicarbonate because of risk of precipitation. Increasing the pH will accelerate the onset of anesthetic action.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Bupivacaine is available in 0.25%, 0.5%, and 0.75% (2.5, 5 and 7.5 mg/mL) solution for injection. Exparel, local multivesicular liposomes are available in a bupivacaine concentration of 13.3 mg/mL in 10- or 20-mL vials.

**Stability and Storage**

Store in a tightly sealed container at room temperature. Avoid mixing with strongly acidic or alkaline solutions. If solutions change to a yellow, pink, or darker color, they should not be used. If pH is adjusted by mixing with alkalinizing solutions (e.g., bicarbonate), the drug is stable but must be used soon after mixing.

**Small Animal Dosage****Dogs and Cats**

- Epidural dose: 1-1.5 mg/kg; for nerve blocks, usually 0.2 mL/kg of 0.5% solution is used.
- Multivesicular liposomes: Infiltrate surgical site with 100-200 mg per site. Duration of effect is usually 96 hours.

**Large Animal Dosage**

- Limited to local infiltration for minor surgery.

**Regulatory Information**

No withdrawal times are established for animals intended for food (extralabel use). When used for local infiltration, clearance from the animal is expected to be rapid. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).  
RCI Classification: 2

## Buprenorphine Hydrochloride

byoo-preh-nor'feen hye-droe-klor'ide

**Trade and other names:** Buprenex, Vetergesic (UK formulation). Simbadol, Butrans (human transdermal form)

**Functional classification:** Analgesic, opioid

### Pharmacology and Mechanism of Action

Opioid analgesic. Buprenorphine is a partial mu-receptor agonist and kappa-receptor antagonist. It is a thebaine derivative and was originally developed in the 1970s as a treatment for opiate addiction in people because of its properties as a mu-receptor partial agonist. It is 25 to 50 times more potent than morphine. It has higher binding affinity for the opiate receptor, which may prolong the effects. However, it has a delayed onset of activity, and because of its property as a partial mu-opiate agonist, it has moderate analgesia with a ceiling effect. Buprenorphine has fewer adverse effects than other opiates and may cause less respiratory depression than other opiates. The pharmacokinetics in dogs have been variable, depending on the study. The half-life in dogs has ranged from 4 hours to 9 hours, with a clearance from 5.4-24 mL/kg/min. The pharmacokinetics in cats have been studied extensively. The half-life from IV administration is 7-10 hours. Transmucosal (sublingual) absorption in cats has been previously reported to be over 100%; however, more recent studies indicate that this value may be overestimated and that 23%-32% absorption from this route may be more likely. In horses the half-life is 7 hours, with a clearance of 8 mL/kg/min, and the absorption from IM administration is highly variable (41%-93%).

### Indications and Clinical Uses

Buprenorphine is an opiate analgesic that is used for pain control in dogs, cats, horses, and some exotic and zoo species. It has lower efficacy (lower ceiling) than pure mu-receptor agonists such as morphine. Buprenorphine has been shown to be effective in animal studies for treating postoperative pain. Duration of analgesia based on plasma values in animals is 3-4 hours, but it may be longer clinically because of slow dissociation from binding sites and higher affinity for the mu-receptor, or longer half-life in the central nervous system. Duration of effect has not been established for all indications in well-controlled studies and has been variable. It may have a longer time to the onset of effect compared to other opiates.

In cats, it has been administered for transmucosal absorption (buccal administration), at a dose of 20 mcg/kg (0.02 mg/kg), and reported to be effective in some studies. However, other studies have shown lower absorption of 23%-32% from transmucosal delivery in cats and lower efficacy; therefore, higher doses of 0.04 mg/kg (40 mcg/kg) transmucosal delivery may be needed every 8 hours to control pain in many cats. At low doses (0.01-0.02 mg/kg, or 10-20 mcg/kg) in cats, the IM or IV route of administration is more effective than the SQ route. In dogs, absorption from transmucosal (gingival) administration is less complete (47%) and higher doses must be administered to achieve analgesic effects. In dogs, 120 mcg/kg administered transmucosal (gingiva) is equivalent to 20 mcg/kg intravenously. At these doses for dogs, the high volume increases the risk of drug loss from the mouth or from swallowing.

Buprenorphine patches for transdermal administration (Butrans) have been used in dogs at a dose of 70 mcg/hour, which was equivalent to a SQ dose of 20 mcg/kg. The patch has a slow onset (17 hours lag time), but a duration of 7 days. However, a 35 mcg/hr patch in cats did not produce antinociceptive effects and plasma drug levels were not detected until 36 hours post-placement of the patch.

A concentrated solution (1.8 mg/mL) is available for administration SQ to cats at a dose of 0.24 mg/kg (240 mcg/kg) once per day. Buprenorphine-SR is available as a sustained-release biodegradable polymer designed to produce effective concentrations for 72 hours. Injection of Buprenorphine-SR in dogs produced concentrations over 1 ng/mL for over 72 hours at a dose of 270 mcg/kg SQ.

In horses, the doses that are analgesic are likely to produce adverse effects (excitement and locomotor activity), which limits the use in horses unless it is administered with sedatives and other analgesics. The adverse effects in horses persist longer than the analgesic effects.

In people, buprenorphine analgesia has been enhanced with the addition of small doses of naloxone (0.001-0.1 mcg/kg), but this effect has not been investigated in animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are similar to other opiate agonists, except there may be less respiratory depression. Sedation is common. Dependency from chronic use of buprenorphine may be less than with pure agonists. Lethal dose in dogs (80 mg/kg) is much higher than the therapeutic dose.

In horses, restlessness, excitatory reactions, head shaking, pawing, shifting leg movements, decreased intestinal motility, and increased locomotor activity are likely and may persist for several hours.

#### Contraindications and Precautions

Patients receiving buprenorphine may require higher doses of naloxone for reversal. IV dose in horses may cause behavior reactions (excitement, pacing). There are formulations that vary greatly in concentration from 0.3 mg/mL to 1.8 mL (Simbadol); therefore, pay close attention to the concentration of the formulation to avoid overdoses.

#### Drug Interactions

As a partial agonist, it may reverse or antagonize some of the mu-receptor effects of other opiates, such as morphine or fentanyl.

### Instructions for Use

Buprenorphine is used for analgesia, often in combination with other analgesics or in conjunction with general anesthesia. It has been used safely with acepromazine and alpha-2 agonists as a pre-anesthetic. It is longer acting than morphine and only partially reversed by naloxone. When administration is intended to be buccal (trans-mucosal), it is important that the entire dose be applied to the oral mucosa and not swallowed. Ingested drug will not be effective (only 3%-6% oral absorption). Therefore as the dose increases, the volume also increases and there is a higher likelihood that some of the drug will be lost from the mouth or swallowed (e.g., at a dose of 0.03 mg/kg to cats, the volume necessary for administration is 0.45 mL per average cat).

### Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, if necessary, atropine can be administered. If serious respiratory depression occurs, the opioid can be reversed with naloxone. Patients receiving buprenorphine may require higher doses of naloxone for reversal. Although plasma or serum concentrations are not typically measured, levels of 4-10 ng/mL have been associated with analgesic efficacy.

**Formulations**

- Buprenorphine is available in 0.3-mg/mL injection solution in a 1-mL vial. Simbadol is a veterinary formulation concentrated in 1.8 mg/mL for use in cats. Human formulations include 8-mg sublingual tablets (Subutex and Suboxone with naloxone), which has been used in people to treat substance abuse. Suboxone (with naloxone) is also available in a transmucosal/sublingual film.
- Butrans is a 7 day transdermal system that delivers 5-, 10-, and 20-mcg/hour to human patients.
- Buprenorphine-SR is available as an injectable sustained-release polymer that is designed for 72 hour delivery in a 10 mg/mL or 3 mg/mL formulation.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Use sodium chloride for infusions. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- 0.006-0.02 mg/kg q4-8h IV, IM, or SQ. For analgesia, doses have been increased to as high as 0.03-0.04 mg/kg SQ.
- Constant rate infusion (CRI): 20 mcg/kg IV, followed by 5 mcg/kg/hour infusion.
- Epidural: 0.003-0.006 mg/kg (3-6 mcg/kg).
- Buprenorphine SR: 120-270 mcg/kg (0.12-0.27 mg/kg) SQ (duration of 72 hours).

**Cats**

- For analgesia, a dose of 0.01-0.02 mg/kg (10-20 mcg/kg) IV or 0.02 mg/kg (20 mcg/kg) IM. Duration is 4-6 hours typically. Additional doses of 0.02 mg/kg may be administered.
- Constant rate infusion (CRI): 20 mcg/kg IV, followed by 12 mcg/kg/hour infusion.
- Subcutaneous administration: The concentrated formulation (Simbadol can be administered SQ once daily for up to 3 days at a dose of 0.24 mg/kg (240 mcg/kg). This formulation may be administered prior to surgery.
- Buccal (transmucosal) administration: 0.02-0.04 mg/kg (20-40 mcg/kg) q8h. 0.02 mg/kg (20 mcg/kg) is equivalent to 0.066 mL per kg. This may be applied to the cat's gingival or oral mucosa (i.e., sublingual).
- Epidural: 12.5 mcg/kg diluted with saline to a volume of 0.3 mL/kg.
- Buprenorphine SR: 120 mcg/kg-270 mcg/kg (0.12-0.27 mg/kg) SQ (duration of 72 hours).

**Large Animal Dosage****Horses**

- 0.005-0.01 mg/kg (5-10 mcg/kg IM); short acting in horses.

**Sheep**

- 0.01 mg/kg (10 mcg/kg) IM, q6h.

**Regulatory Information**

The drug is controlled by the Drug Enforcement Administration (DEA). Do not administer to animals intended for food.

Schedule III controlled drug.

RCI Classification: 2

## Buspirone Hydrochloride

byoo-speer'own hye-droe-klor'ide

**Trade and other names:** BuSpar

**Functional classification:** Behavior modification

### Pharmacology and Mechanism of Action

Antianxiety agent of the azapirone class. Buspirone acts as a direct-acting serotonin (5-HT<sub>1A</sub>) agonist. By activating 5HT<sub>1A</sub> receptors, buspirone and related drugs alter mood and anxiety. Buspirone is used to treat anxiety and other behavior problems. Other related drugs include gepirone and ipsapirone.

### Indications and Clinical Uses

In veterinary medicine, buspirone has been primarily used for the treatment of urine spraying (urine marking) in cats. In cats, there are published studies demonstrating efficacy. However, some cats relapse after treatment is discontinued. Buspirone also has been used as an antiemetic in cats (4 mg/kg SQ). In dogs, it has occasionally been used to treat behavior problems, such as anxiety disorders.

### Precautionary Information

#### Adverse Reactions and Side Effects

Few side effects are seen in cats compared to other drugs. Some cats show increased aggression; and some cats show increased affection and friendliness to owners. It may produce mild sedation.

#### Contraindications and Precautions

Do not use in animals with sensitivity to serotonin agonists.

#### Drug Interactions

Do not use with other serotonin antagonists, selective serotonin reuptake inhibitors (SSRIs), or MAOIs (e.g., selegiline).

### Instructions for Use

Some efficacy trials suggest effectiveness for treating urine spraying in cats. There may be a lower relapse rate compared to other drugs.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Buspirone is available in 5-, 10-, 15- and 30-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Cats

- 2.5-5 mg/cat q12h PO, which may be increased to 5-7.5 mg per cat twice daily for some cats (0.5-1 mg/kg q12h PO).

#### Dogs

- 2.5-10 mg/dog q24h or q12h PO.
- 1 mg/kg q12h PO.

**Large Animal Dosage**

**Horses**

- 100-250 mg/horse q24h PO (0.5 mg/kg).

**Regulatory Information**

Do not administer to animals intended for food.

RCI Classification: 2

**Busulfan**

byoo-sul'fan

**Trade and other names:** Myleran

**Functional classification:** Anticancer agent

**Pharmacology and Mechanism of Action**

Anticancer agent. Busulfan is a bifunctional alkylating agent and acts to disrupt DNA of tumor cells.

**Indications and Clinical Uses**

Busulfan is used primarily for lymphoreticular neoplasia.

**Precautionary Information**

**Adverse Reactions and Side Effects**

Leukopenia is the most severe side effect.

**Contraindications and Precautions**

Do not use in animals with suppressed bone marrow.

**Drug Interactions**

No drug interactions are reported in animals.

**Instructions for Use**

Busulfan is usually used in combination with other anticancer agents. Consult specific protocol for details.

**Patient Monitoring and Laboratory Tests**

Monitor CBC in animals during treatment.

**Formulations**

- Busulfan is available in 2-mg tablets, and a 6 mg/ml injection under the name Busulfex.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage**

**Dogs and Cats**

- 3-4 mg/m<sup>2</sup> q24h PO.

**Large Animal Dosage**

- No dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in food animals because it is an anticancer agent.

## Butorphanol Tartrate

byoo-tor'fah-nole tar'trate

**Trade and other names:** Torbutrol, Dolorex, Butorphine, and Torbugesic

**Functional classification:** Analgesic, opioid

## Pharmacology and Mechanism of Action

Opioid analgesic. Opiate that acts as kappa receptor agonist and weak mu-receptor antagonist (some authorities classify the antagonist effect as a “partial agonist” effect). As a kappa agonist, butorphanol produces sedation and analgesia in animals. It is considered a mild analgesic compared to pure mu-receptor opiates. It is often used in combination with other anesthetics. It has a short half-life in animals (1-2 hours) and a short duration of analgesia (1-2 hours).

## Indications and Clinical Uses

Butorphanol is used for perioperative analgesia, for chronic pain, and as an antitussive agent. It is considered a weak analgesic compared to drugs that are pure mu-receptor agonists, and some of the observed effects may be caused by sedation rather than analgesia. In dogs, at doses of 0.4 mg/kg, butorphanol produces analgesia for a duration of 1 hour or less. As an antitussive, it is more potent than morphine (4×) and codeine (100×). Duration of the antitussive effect is approximately 90 minutes, but the effect may persist for as long as 4 hours. In horses, it may be administered IV, IM, and as a constant-rate infusion (CRI). Constant-rate infusion has been shown effective in controlled studies.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are similar to other opioid analgesic drugs. Sedation is common at analgesic doses. Respiratory depression can occur with high doses. Lethal dose in dogs ( $LD_{50}$ ) is 20 mg/kg, which is much higher than clinical doses. Although bradycardia rarely needs to be treated when it is caused by an opioid, if necessary, atropine can be administered. If serious respiratory depression occurs, the opioid can be reversed with naloxone. Dysphoric effects have been observed with agonist/antagonist drugs; this effect has been observed in cats. Decreased intestinal peristalsis and constipation may occur in some animals. A decrease in intestinal motility may be a particular concern in some horses.

### Contraindications and Precautions

Schedule IV controlled substance. Butorphanol use in birds requires much higher doses than in mammals because of shorter half-life and rapid clearance (e.g., 2-4 mg/kg every 2-4 hours).

### Drug Interactions

Butorphanol is compatible with many other analgesics and is used in combination treatment for analgesia. Because butorphanol is an agonist/antagonist, it may



antagonize some effects of drugs that are pure agonists (e.g., fentanyl, morphine, and oxymorphone). However, the clinical significance of this antagonism has been debated among experts. Do not mix with sodium barbiturates.

### Instructions for Use

Butorphanol is often used in combination with anesthetic agents or in conjunction with other analgesic drugs. For most indications, a dose of 0.4 mg/kg is considered optimum, and there is no reason to increase the dose above 0.8 mg/kg because this is considered the ceiling dose. Butorphanol has a short duration of effect of less than 2 hours and usually only 1 hour. In horses, because butorphanol may cause increased locomotor activity and excitement, xylazine may be administered prior to buprenorphine.

### Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration.

### Formulations

- Butorphanol is available in 1-, 5-, and 10-mg tablets and 0.5- and 1-mg/mL injection. Torbugesic is available as a 10 mg/mL injection; Butorphanol for cats is available as a 2-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- Antitussive: 0.055 mg/kg q6-12h SQ, 0.011 mg/kg IM, or 0.5-1 mg/kg q6-12h PO.
- Peanesthetic: 0.2-0.4 mg/kg (with acepromazine) IV, IM, or SQ.
- Analgesic: 0.2-0.4 mg/kg q2-4h IV, IM, or SQ or 1-4 mg/kg q6h PO.
- CRI: Loading dose of 0.2-0.4 mg/kg IV, followed by 0.1-0.2 mg/kg/hr.

#### Cats

- Analgesic: 0.2-0.8 mg/kg q2-6h IV or SQ or 1.5 mg/kg q4-8h PO.
- CRI: Loading dose of 0.2-0.4 mg/kg IV, followed by 0.1-0.2 mg/kg/hr.

### Large Animal Dosage

#### Horses

- Pain: 0.2-0.4 mg/kg q3-4h IV. In some instances, lower doses of 0.02-0.1 mg/kg IV or 0.04-0.2 mg/kg IM have been used. Lower doses of 0.1 mg/kg IV have been used to minimize the decrease in intestinal motility.
- Sedation: 0.01-0.06 mg/kg IV.
- CRI: 13-24 mcg/kg/hr (0.013-0.024 mg/kg) IV.

#### Ruminants

- 0.05-0.2 mg/kg IV.

#### Cattle

- In combination with xylazine: 0.01-0.02 mg/kg IV.

### Regulatory Information

Drug controlled by DEA, Schedule IV.

Do not administer to animals intended for food.

RCI Classification: 2

## N-Butylscopolammonium Bromide (Butylscopolamine Bromide)

en-byoo-til-skoe-pahl'ah-moe-nee-um broe'mide

**Trade and other names:** Buscopan

**Functional classification:** Antispasmodic

### Pharmacology and Mechanism of Action

Antispasmodic, antimuscarinic, anticholinergic drug. This is a quarternary ammonium compound derived from belladonna alkaloid. Butylscopolamine, like other antimuscarinic drugs, blocks cholinergic receptors and produces a parasympatholytic effect. It affects receptors throughout the body, but it is used more commonly for its gastrointestinal effects. It effectively inhibits secretions and motility of the gastrointestinal tract by blocking parasympathetic receptors. It has a short half-life (15-25 minutes) and short duration of action. As a quarternary ammonium compound, it typically does not cross the blood-brain barrier to produce central nervous system reactions.

### Indications and Clinical Uses

Butylscopolamine bromide is indicated for treating pain associated with spasmodic colic, flatulent colic, and intestinal impactions in horses. It is also used to relax the rectum and reduce intestinal strain to facilitate diagnostic rectal palpation.

This agent also relieves bronchoconstriction caused by airway smooth muscle contraction mediated by vagal activation of muscarinic receptors.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse reactions from anticholinergic drugs are related to their blocking of acetylcholine receptors and producing a systemic parasympatholytic response. As expected with this class of drugs, animals will have increased heart rate, decreased secretions, dry mucous membranes, decreased gastrointestinal tract motility, and dilated pupils. The effects on intestinal motility usually have less than 2 hours' duration. In target animal safety studies in which doses of 1, 3, and 5 times the approved dose and up to 10 times the dose were administered to horses, the clinical signs described previously were observed. However, at high doses there were no CBC or biochemical abnormalities or lesions identified at necropsy.

#### Contraindications and Precautions

N-butylscopolammonium bromide will decrease intestinal motility. Use cautiously in conditions where decreased motility will be a concern.

#### Drug Interactions

N-butylscopolammonium bromide is an anticholinergic drug and therefore will antagonize any other medications that are intended to produce a cholinergic response (e.g., metoclopramide).

### Instructions for Use

Experience is limited to treating spasmodic colic, flatulent colic, and intestinal impactions in horses. There is no experience in other animals.

### Patient Monitoring and Laboratory Tests

Monitor equine intestinal motility (gut sounds and fecal output) during treatment. Monitor heart rate in treated animals.

## 96 N-Butylscopolammonium Bromide (Butylscopolamine Bromide)

### Formulations

- N-butylscopolammonium is available in a 20-mg/mL solution.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

- No dose is reported for small animals.

### Large Animal Dosage

#### Horses

- 0.3 mg/kg, slowly IV as a single dose (1.5 mL per 100 kg). Onset of action is usually within 2 minutes, with a duration of less than 2 hours.
- To relieve bronchoconstriction: 0.3 mg/kg IV, single dose

### Regulatory Information

Do not administer to animals intended for food.

## Calcitriol

kal-sih-trye'ole

**Trade and other names:** Rocaltrol and Calcijex

**Functional classification:** Calcium supplement

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### Pharmacology and Mechanism of Action

Vitamin D analogue, also called *1,25-dihydroxycholecalciferol*. Calcitriol is normally formed in the kidneys from 25-hydroxycholecalciferol. Action of calcitriol is to increase calcium absorption from the intestine and facilitate a parathyroid hormone (PTH) effect on bone. Low calcitriol levels in animals can cause decreased intestinal calcium absorption. Animals with chronic kidney disease (especially cats) and hyperparathyroidism often have low calcitriol levels. Calcitriol can also inhibit synthesis and storage of PTH.

### Indications and Clinical Uses

Calcitriol is used to treat calcium deficiency and diseases such as hypocalcemia associated with hyperparathyroidism. It is also used to increase calcium in cats that have had parathyroid glands removed. In this use, it is often administered with calcium supplements to the diet. It is used in dogs and cats to manage calcium and phosphorous balance with chronic kidney disease. Although used by veterinarians to reduce renal secondary PTH concentrations in animals with chronic kidney disease, this benefit is more controversial and not supported by strong evidence. Supplementation to cats with chronic kidney disease may help slow progression of disease in some cats; but, the treatment is controversial and some cats do not show a benefit. Calcitriol should not be used as a vitamin D supplement.

### Precautionary Information

#### Adverse Reactions and Side Effects

Overdose can result in hypercalcemia. High doses can cause soft-tissue mineralization.

#### Contraindications and Precautions

Do not use in patients that are at risk of hypercalcemia. Capsules made for humans may contain high overdoses for dogs and cats and should be reformulated.

#### Drug Interactions

Calcitriol may cause hypercalcemia if used with thiazide diuretics.

### Instructions for Use

When comparing doses to Vitamin D, 1 unit of Vitamin D is equivalent to 0.025 mcg cholecalciferol or ergocalciferol (400 units of Vitamin D = 10 mcg of cholecalciferol). Doses should be adjusted in each patient according to response and monitoring calcium plasma concentration. Dose requirements may vary depending on the adjustment to calcium levels. For example, when used for treating dogs with chronic kidney disease, the dose was 2.5 ng/kg/day, but ranged from 0.75 to 5 ng/kg/day based on adjustments from measuring calcium concentrations. When used in chronic renal failure, it is often used with intestinal phosphate binders (e.g., aluminum hydroxide) and dietary phosphorous restriction. Recommended phosphate concentrations should be maintained < 6 mg/dL. In cats, do not administer with a meal. It is best administered in the evening before a meal. If ionized calcium becomes increased above reference range (above 4.5-5.5 mg/dL), stop treatment, then reintroduce at a lower dose.

### Patient Monitoring and Laboratory Tests

Monitor plasma ionized calcium concentration. Adjust doses as necessary to maintain normal calcium, phosphorous, and PTH concentrations. Monitor serum PTH concentrations (assays are available in many diagnostic laboratories). Monitor serum creatinine in animals when used to treat chronic kidney disease.

### Formulations

- Calcitriol is available as injection (Calcijex) in a 1- and 2-mcg/mL and in 0.25- and 0.5-mcg capsules and 1-mcg/mL oral solution (Rocaltrol).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- Renal secondary hyperparathyroidism in chronic renal failure: 2.5 ng/kg, PO, once daily. Adjust dose with calcium and PTH measurements. If PTH concentrations remain elevated and calcium is not elevated, increase the dose to 3.5 ng/kg, once daily. The dose may be increased incrementally up to 5 ng/kg, once daily.

#### Cats

- Hypocalcemia (after removal of parathyroid glands): 0.25 mcg/cat q48h PO or 0.01-0.04 mcg/kg/day PO (10-40 ng/kg/day).
- Renal secondary hyperparathyroidism: 2.5 ng/kg, PO, once daily. Adjust dose with calcium and PTH measurements. If PTH concentrations remain elevated and calcium is not elevated, increase the dose to 3.5 ng/kg, once daily, and incrementally up to a dose of 5 ng/kg/day. Do not exceed 5 ng/kg/day.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

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## Calcium Carbonate

**Trade and other names:** Titralac, Calci-mix, Tums, and generic brands

**Functional classification:** Calcium supplement

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### Pharmacology and Mechanism of Action

Calcium supplement. Calcium is essential for the functional integrity of several body systems. Calcium carbonate is equivalent to 400 mg of calcium ion per gram. Calcium carbonate neutralizes stomach acid for treating and preventing stomach ulcers.

### Indications and Clinical Uses

Calcium carbonate is used as an oral calcium supplement for hypocalcemia, sometimes used with vitamin D supplements or calcitriol. It contains 40% elemental calcium. It is used as antacid to treat gastric hyperacidity and gastrointestinal (GI) ulcers and as an intestinal phosphate binder for hyperphosphatemia associated with renal failure.

Pronefra (calcium carbonate and magnesium carbonate) is administered as a palatable phosphate binder in dogs and cats. It is administered as an oral liquid suspension with meals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Few side effects. High calcium concentrations are possible. With any calcium supplements, constipation and intestinal bloating can occur.

#### Contraindications and Precautions

Do not administer to animals predisposed to forming calcium-containing renal or cystic calculi. When calcium carbonate or calcium citrate is used as a phosphate binder to prevent hyperphosphatemia, caution is advised to avoid hypercalcemia in patients with renal failure.

#### Drug Interactions

Oral administration of calcium supplements may interfere with absorption of other drugs such as fluoroquinolones (e.g., enrofloxacin, orbifloxacin, marbofloxacin, and pradofloxacin), bisphosphonates, zinc, iron, and tetracyclines. Use cautiously with thiazide diuretics because this could cause a high increase in calcium concentrations.

### Instructions for Use

Calcium carbonate is equivalent to 400 mg of calcium ion per gram. Doses are primarily derived from extrapolation of human doses. When used as a calcium supplement, doses should be adjusted according to serum calcium concentrations. Administer with food to improve oral absorption. Some tablets also contain vitamin D. Doses are based on calcium carbonate, not the ion concentration (e.g., a 650-mg tablet contains 260 mg of calcium ion).

### Patient Monitoring and Laboratory Tests

Monitor serum calcium levels, particularly if patients have renal failure.

### Formulations

Calcium carbonate is available in tablets or oral suspension, most of which are over-the-counter (OTC). One gram of calcium carbonate is equivalent to 400 mg of calcium ion. Calci-mix is available in 1.25-g capsules. Over-the-counter tablets are available in 500 and 600 mg and 1, 1.25, and 1.5 g. Oral suspension (Titalac) is 1.25 g per 5 mL. The formulation Pronefra also is available as calcium carbonate and magnesium carbonate. It is an oral syrup that may be administered as a phosphate binder in cats. Pronefra is a palatable liquid suspension with poultry liver flavoring.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

### Small Animal Dosage

#### Dogs and Cats

- Calcium supplementation: 70-185 mg/kg/day given with food PO.
- Phosphate binder: 60-100 mg/kg/day in divided doses, usually given with food PO.
- Pronefra (calcium carbonate and magnesium carbonate) for use as a phosphate binder. Administer with a meal. Cats: 1 mL per 4.4 kg (8.8 lb), twice a day at mealtime. Dogs: 1 mL per 5 kg (11 pounds), twice a day at mealtime.

## 100 Calcium Chloride

### Large Animal Dosage

- No dose has been reported for large animals. Usually, other calcium salts are used for supplementation in cattle.

### Regulatory Information

No withdrawal times are available. Because this is a normal dietary supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

## Calcium Chloride

**Trade and other names:** Generic brands

**Functional classification:** Calcium supplement

### Pharmacology and Mechanism of Action

Calcium supplement. Calcium is essential for the functional integrity of several body systems. Injection is 27.2 mg of calcium ion (1.36 mEq) per mL. Calcium chloride increases ionized calcium in blood greater than do other calcium salts.

### Indications and Clinical Uses

Calcium chloride is used in acute situations to supplement as electrolyte replacement or as a cardiotonic. It is administered to cows for hypocalcemia (milk fever).

### Precautionary Information

#### Adverse Reactions and Side Effects

Overdose with calcium is possible. Do not administer intravenous solution SQ or IM because it may cause tissue necrosis.

#### Contraindications and Precautions

Do not administer by IV injection at a rapid rate. Rapid IV administration to cows can cause cardiac arrhythmias and even death.

#### Drug Interactions

Calcium chloride will precipitate with sodium bicarbonate. Do not mix with compounds known to chelate with calcium.

### Instructions for Use

Injection is 27.2 mg of calcium ion (1.36 mEq) per mL. It is usually used in emergency situations. Intracardiac administrations have been performed, but avoid injections into the myocardium.

### Patient Monitoring and Laboratory Tests

Monitor serum calcium concentration. Monitor heart rhythm during administration.

### Formulations

- Calcium chloride is available in a 10% (100-mg/mL) solution. This supplies 1.36 mEq calcium ion per mL. Preparations for cattle usually contain 8.5-11.5 g calcium per 500 mL. Many formulations also contain magnesium.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

## Small Animal Dosage

### Dogs and Cats

- 0.1-0.3 mL/kg IV (slowly).

## Large Animal Dosage

### Cows

- 2 grams/100 kg body weight, IV at a rate of 1 g/min.

### Horses

- 1-2 grams per adult horse IV slowly.

## Regulatory Information

No withdrawal times are available. Because this is a normal supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

## Calcium Citrate

**Trade and other names:** Citracal (OTC)

**Functional classification:** Calcium supplement

## Pharmacology and Mechanism of Action

Calcium supplement. Calcium is essential for the functional integrity of several body systems. It is administered orally to supply calcium to the diet.

## Indications and Clinical Uses

Calcium citrate is used in the treatment of hypocalcemia, such as with hypoparathyroidism. It contains 21% elemental calcium. It also is used as an intestinal phosphate binder for hyperphosphatemia associated with renal failure.

## Precautionary Information

### Adverse Reactions and Side Effects

Hypercalcemia is possible with oversupplementation. With any calcium supplements, constipation and intestinal bloating can occur. Constipation and bloating is more likely with calcium citrate than calcium carbonate.

### Contraindications and Precautions

When calcium carbonate or calcium citrate is used as a phosphate binder to prevent hyperphosphatemia, caution is advised to avoid hypercalcemia in patients with renal failure.

### Drug Interactions

Oral administration of calcium supplements may interfere with absorption of other drugs such as fluoroquinolones (e.g., enrofloxacin, orbifloxacin, marbofloxacin), bisphosphonates, zinc, iron, and tetracyclines. Calcium citrate does not require acid for absorption and may be administered with ulcer drugs that suppress stomach acid (e.g., omeprazole, H-2 blockers).

## Instructions for Use

Doses should be adjusted according to serum calcium concentration. It does not have to be administered with meals, as does calcium carbonate.



## 102 Calcium Gluconate and Calcium Borogluconate

### Patient Monitoring and Laboratory Tests

Monitor serum calcium levels, particularly if patients have renal failure. If used as a phosphate binder, adjust doses based on serum phosphorous concentrations.

### Formulations

- Calcium citrate is available in 950-mg tablets (contains 200 mg of calcium ion), and 1,000 mg tablets. Some forms also contain Vitamin D<sub>3</sub>.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

### Small Animal Dosage

#### Cats

- 10-30 mg/kg q8h (with meals) PO.

#### Dogs

- 20 mg/kg/day (with meals) PO.

#### Dogs and Cats

- Phosphate binder (to prevent hyperphosphatemia): 10-20 mg/kg per day in divided doses, with meals PO.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No withdrawal times are available. Because this is a normal dietary supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

## Calcium Gluconate and Calcium Borogluconate

**Trade and other names:** Kalcinate, AmVet, Cal-Nate, and generic brands

**Functional classification:** Calcium supplement

### Pharmacology and Mechanism of Action

Calcium supplement. Calcium is essential for the functional integrity of several body systems. It is administered orally to supply calcium to the diet, but injected for acute conditions in which a rapid increase in serum calcium is needed. Calcium gluconate contains 9% elemental calcium.

### Indications and Clinical Uses

Calcium gluconate and calcium borogluconate are used in the treatment of hypocalcemia, such as with hypoparathyroidism but are used less common than other forms. They are used in electrolyte deficiency. Calcium supplements are administered to cattle for treatment of hypocalcemia (milk fever).

### Precautionary Information

#### Adverse Reactions and Side Effects

Hypercalcemia is possible with oversupplementation. Calcium supplements may cause constipation. SQ or IM injections of calcium salts may cause tissue injury and necrosis at the site of injection.

### Contraindications and Precautions

Avoid rapid IV administration. Avoid use in patients that are prone to calcium-containing renal or cystic calculi. Avoid administration of IV solution IM or SQ because it will cause tissue necrosis.

### Drug Interactions

Do not mix with any bicarbonate (sodium bicarbonate), phosphates, sulfates, and tartrates because it may precipitate. Specific drugs that can precipitate with calcium gluconate include oxytetracycline, promethazine, sulfamethazine, tetracycline, cephalothin, and amphotericin B. Calcium supplements may interfere with the oral absorption of iron, tetracyclines, and fluoroquinolones.

### Instructions for Use

The 500-mg tablets contain 45 mg of calcium ion. The 10% injection contains 97 mg (9.3 mg of calcium ion [0.47 mEq]) per mL.

### Patient Monitoring and Laboratory Tests

Monitor serum calcium concentration. Monitor heart rate during IV administration.

### Formulations

- Calcium gluconate is available as 10% (100-mg/mL) injection. Calcium gluconate 10% contains 9.3 mg of calcium ion per mL, or 0.465 mEq per mL. Calcium gluconate is available in tablets in sizes of 325, 500, 650, 975 mg, and 1 g. Each gram contains 90 mg of calcium ion. Chewable tablets intended for human use are available in 650-mg and 1-g tablets.
- Calcium borogluconate is available as 230 mg/mL (AmVet Calcium Gluconate 23% and Cal Nate).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Solutions should be clear. If crystals are present, warm vial up to 30-40° C (86-104° F) to dissolve crystals. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

### Small Animal Dosage

#### Dogs and Cats

- 75-500 mg IV, slowly.

### Large Animal Dosage (Use Calcium Borogluconate)

#### Cattle and Horses

- 5-12 grams, diluted in 500 mL and infused IV, slowly.

#### Pigs and Sheep

- 5-1.5 grams IV, slowly.

#### Dairy Cows

- 2 grams/100 kg body weight, slowly, at a rate of 1 g/min.

#### Horses

- 50-70 mg/kg, diluted in 5% dextrose and infused slowly, IV.

### Regulatory Information

No withdrawal times are available. Because this is a normal dietary supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

## Calcium Lactate

**Trade and other names:** Generic brands

**Functional classification:** Calcium supplement

### Pharmacology and Mechanism of Action

Calcium supplement. Calcium is essential for the functional integrity of several body systems. This oral supplement is used to provide animals with dietary calcium to prevent or treat a deficiency. Contains 13% elemental calcium.

### Indications and Clinical Uses

Calcium lactate is used in treatment of hypocalcemia, such as with hypoparathyroidism, and in electrolyte deficiency.

### Precautionary Information

#### Adverse Reactions and Side Effects

Hypercalcemia possible with oversupplementation.

#### Contraindications and Precautions

Avoid use in patients that are prone to calcium-containing renal or cystic calculi.

#### Drug Interactions

Calcium supplements may interfere with the oral absorption of iron, tetracyclines, and fluoroquinolones.

### Instructions for Use

Calcium lactate contains 130 mg of calcium ion per gram.

### Patient Monitoring and Laboratory Tests

Monitor serum calcium concentrations.

### Formulations

- Calcium lactate is available in 325-mg (42.25 mg of calcium ion) and 650-mg (84.5 mg of calcium ion) OTC tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Do not mix with other compounds that may chelate with calcium.

### Small Animal Dosage

#### Dogs

- 0.5 grams/day (500 mg) (in divided doses) PO.

#### Cats

- 0.2-0.5 grams/day (200-500 mg) (in divided doses) PO.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No withdrawal times are available. Because this is a normal dietary supplement with little risk from residues, no withdrawal time is suggested for animals intended for food.

## Captopril

kap'toe-pril

**Trade and other names:** Capoten

**Functional classification:** Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

C

### Pharmacology and Mechanism of Action

Angiotensin-converting enzyme inhibitor. Captopril inhibits conversion of angiotensin I to angiotensin II, leading to vasodilation. Angiotensin II is a potent vasoconstrictor and will stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. Angiotensin-converting enzyme inhibitors limit the ability of aldosterone to cause sodium and water retention that contribute to congestion. Captopril, like other ACE inhibitors, will cause vasodilation, but ACE inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins.

### Indications and Clinical Uses

Captopril, like other ACE inhibitors, is used to treat hypertension and congestive heart failure (CHF). It has been used primarily in dogs, but its use has declined. Captopril is the first ACE inhibitor available for clinical use, but has been replaced by other ACE inhibitors such as enalapril, benazepril, and lisinopril. Unlike benazepril and enalapril, it has not been studied for clinical use in dogs and cats.

### Precautionary Information

#### Adverse Reactions and Side Effects

Hypotension is possible with excessive doses. Captopril may cause azotemia in some patients, especially when administered with potent diuretics (e.g., furosemide). Gastrointestinal side effects, predominantly anorexia, are common in dogs.

#### Contraindications and Precautions

Discontinue ACE inhibitors in pregnant animals; they cross the placenta and have caused fetal malformations and death of the fetus.

#### Drug Interactions

Use cautiously with diuretics and potassium supplements. Nonsteroidal anti-inflammatory drugs (NSAIDs) may diminish antihypertensive effect.

### Instructions for Use

Use of captopril has been replaced by enalapril and benazepril in small animal practices, and most clinical experts recommend these other drugs instead of captopril.

### Patient Monitoring and Laboratory Tests

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

### Formulations

- Captopril is available in 12.5-, 25-, 50-, and 100-mg tablets.

### Stability and Storage

Store in a tightly sealed container at room temperature. More stable at acidic pH. Oral compounded solutions are stable for 30 days refrigerated. However, tap water should not be used; purified water is necessary to ensure stability.

## Small Animal Dosage

### Dogs

- 0.5-2 mg/kg q8-12h PO.

### Cats

- 3.12-6.25 mg/cat q8h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

Racing Commissioners International (RCI) Classification: 3

## Carbenicillin

kar-ben-ih-sill'in

**Trade and other names:** Formulations previously marketed were Geopen, Pyopen, and carbenicillin indanyl sodium

**Note:** Carbenicillin is no longer commercially available. Information is included here on the pharmacology and clinical use, but other agents should be substituted for clinical use (e.g., piperacillin-tazobactam).

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Carbenicillin has an action similar to ampicillin, which inhibits bacterial cell wall synthesis. Carbenicillin has a broad spectrum of activity that includes both gram-positive and gram-negative bacteria. However, resistance is possible, especially among beta-lactamase-positive strains. The difference between carbenicillin and ampicillin is that it is active against *Pseudomonas aeruginosa* and other gram-negative bacteria that are resistant to ampicillin and amoxicillin. Half-life is short and clearance is rapid in animals; therefore it requires frequent administration.

## Indications and Clinical Uses

Carbenicillin has been used to treat gram-negative infections in animals, including infections caused by *P. aeruginosa*. Carbenicillin has been discontinued and is no longer available. It has been replaced by other broad-spectrum agents such as piperacillin-tazobactam.

## Precautionary Information

### Adverse Reactions and Side Effects

Carbenicillin, like other penicillin drugs, may cause allergy. Carbenicillin may cause bleeding problems in some animals by interfering with platelets.

### Contraindications and Precautions

Use cautiously in patients sensitive to penicillins (e.g., allergy).

### Drug Interactions

No drug interactions are reported in animals. Do not mix in vial with other drugs because inactivation may result.

## Instructions for Use

Carbenicillin has a short half-life and should be administered frequently for optimum bactericidal effect. Carbenicillin injection often is administered with an aminoglycoside when treating *Pseudomonas* infections. Do not mix with aminoglycosides prior to administration, or inactivation will result. Carbenicillin indanyl sodium is the oral formulation of carbenicillin, but attains concentrations that are only sufficient for treating urinary tract infections (UTIs). Do not use for systemic infections.

## Patient Monitoring and Laboratory Tests

Culture and sensitivity testing recommended to guide therapy. Clinical and Laboratory Standards Institute (CLSI) break points are  $\leq 128$  mcg/mL when testing for *Pseudomonas*-susceptible organisms and  $\leq 16$  mcg/mL for other gram-negative organisms.

## Formulations

- Carbenicillin has been unavailable because other drugs are used as a replacement. However, older formulations include 1-, 2-, 5-, 10-, and 30-g vials for injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stable at pH of 6.5, but rate of degradation is greater at higher or lower pH. Use quickly after reconstitution of vials for injection.

## Small Animal Dosage

### Dogs and Cats

- Carbenicillin: 40-50 mg/kg and up to 100 mg/kg q6-8h IV, IM, or SQ.
- Carbenicillin indanyl sodium: 10 mg/kg q8h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Carbimazole

kar-bih'mah-zole

**Trade and other names:** Neomercazole, Vidalta

**Functional classification:** Antithyroid drug

## Pharmacology and Mechanism of Action

Antithyroid drug similar to methimazole. It is a prodrug converted to methimazole after administration. Ten mg of carbimazole is equivalent to 6 mg methimazole. Like methimazole, the action is to serve as substrate for thyroid peroxidase (TPO) and inhibits it and decreases incorporation of iodide into tyrosine molecules. It also inhibits coupling of monoiodinated and di-iodinated residues to form  $T_4$  and  $T_3$ . Carbimazole has been preferred in some patients because, compared to methimazole, it may have fewer side effects, such as less frequent GI problems. Oral absorption (based on methimazole concentrations) is 88% in cats with a half-life of approximately 5 hours.

## Indications and Clinical Uses

Carbimazole has been used for treating hyperthyroidism, primarily in cats. Carbimazole has been more readily available in Europe, where there is more clinical experience, than in the US. Experience in the US is limited because of lack of availability. Sustained-release formulation in Europe (Vidalta) is administered to people as 15 mg once per day, followed by 10-25 mg once daily.

### Precautionary Information

#### Adverse Reactions and Side Effects

In cats, lupuslike reactions are possible, such as vasculitis and bone marrow changes. In people, it has caused agranulocytosis and leukopenia. Other systemic effects reported for methimazole are expected to be similar for carbimazole (for example, bone marrow effects). See methimazole section for additional information.

#### Contraindications and Precautions

Do not use in cats with bone marrow suppression or thrombocytopenia.

#### Drug Interactions

No drug interactions are reported in animals.

## Instructions for Use

Carbimazole is used in Europe; clinical experience in US is limited. Otherwise, the clinical indications and use are similar as for methimazole.

## Patient Monitoring and Laboratory Tests

Monitor thyroid concentrations to adjust dose. Monitor complete blood count (CBC) periodically for evidence of bone marrow suppression.

## Formulations

- This drug has not been approved in the US. This drug has been obtained in Europe.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is not stable in transdermal compounded formulations.

## Small Animal Dosage

### Cats

- 5 mg per cat q8h (induction), followed by 5 mg/cat q12h PO. In Europe, Vidalta (a newer sustained-release brand available) induction usually 15 mg once daily and maintenance dose ranges between 10 mg and 25 mg once daily.

### Dogs

- No dose has been established for dogs.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

## Carboplatin

kar-boe-plat' in

**Trade and other names:** Paraplatin, and generic

**Functional classification:** Anticancer agent

### Pharmacology and Mechanism of Action

Anticancer agent. Carboplatin is a second-generation platinum compound and is related to cisplatin. Action is similar to cisplatin. Its action is a bifunctional alkylating agent, which interrupts replication of DNA in tumor cells. It induces a non-cell cycle-dependent tumor cell lysis. Major route of elimination is via the kidneys. It has replaced cisplatin in some anticancer protocols because it may not be as toxic.

### Indications and Clinical Uses

Carboplatin has been used for squamous cell carcinoma and other carcinomas, melanoma, osteosarcomas, and other sarcomas. It has produced a disease-free interval and survival in dogs with osteosarcoma that is similar to other protocols. When used in dogs, myelosuppression has been the most dose-limiting factor. Compared to cisplatin, carboplatin is better tolerated in cats and is preferred. However, bone marrow suppression is the dose-limiting toxicity in cats.

### Precautionary Information

#### Adverse Reactions and Side Effects

Compared to cisplatin, carboplatin is less emetogenic and less nephrotoxic. In dogs, the other most common adverse effects relate to gastrointestinal system toxicity (gastroenteritis, vomiting, anorexia, and diarrhea). The dose-limiting effect is myelosuppression, anemia, leukopenia, or thrombocytopenia. In dogs, nadir of myelosuppression occurs at 14 days, but recovery occurs by 21-28 days. In cats, the nadir is 21 days and recovery occurs by 28 days. Vomiting is not as much of a problem as for cisplatin, but gastrointestinal toxicosis is still a problem, especially in smaller dogs. Because it is excreted by the kidneys, animals with diminished kidney function may have a higher rate of gastrointestinal toxicosis.

#### Contraindications and Precautions

In one study, small dogs were more prone than larger dogs to adverse effects.

#### Drug Interactions

Do not use with other nephrotoxic drugs.

### Instructions for Use

Available for reconstitution for injection. It is stable for 1 month when reconstituted with 5% dextrose. It may be frozen at  $-4^{\circ}\text{C}$  to prolong the stability of a reconstituted vial. Do not use with administration sets containing aluminum because of incompatibility. It is usually administered in specific anticancer protocols; consult oncology protocols for regimen. In dogs, it has been dosed on a milligram per square meter dose, which has produced a higher incidence of adverse effects in smaller dogs compared to larger dogs; however, smaller dogs also were more likely to respond. Carboplatin is excreted by the kidneys; therefore the dose should be decreased in proportion to reduced glomerular filtration rate (GFR) and creatinine clearance.

### Patient Monitoring and Laboratory Tests

Monitoring of CBC and platelets is recommended during treatment.



## 110 Carprofen

### Formulations

- Carboplatin is available in 50-, 150-, and 450-mg vials for injection, and a 10 mg/mL infusion.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stable for 1 month if reconstituted with 5% dextrose solution. It is stable if frozen at  $-4^{\circ}\text{C}$ .

### Small Animal Dosage

#### Dogs

- 300 mg/m<sup>2</sup>, IV, every 3-4 weeks. It is also administered at 300 mg/m<sup>2</sup> for dogs less than 15 kg and 350 mg/m<sup>2</sup> for dogs greater than 15 kg.

#### Cats

- 200-227 mg/m<sup>2</sup>, IV, every 4 weeks for four treatments; for a 4-kg cat, the dose is equivalent to 14.7 mg/kg.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Carprofen

car-proe'fen

**Trade and other names:** Rimadyl, Vetprofen, Zinecarp (Europe), and generic brands

**Functional classification:** Nonsteroidal anti-inflammatory drug

### Pharmacology and Mechanism of Action

Carprofen is an NSAID. Like other drugs in this class, carprofen has analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by an NSAID is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy gastrointestinal tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. (There may be crossover of COX-1 and COX-2 effects in some situations.) Carprofen is relatively COX-1 sparing compared to older NSAIDs, but it is not known if the specificity for COX-1 or COX-2 determines efficacy or safety. In horses, carprofen is not as COX-2 selective as it is in dogs. As an analgesic agent, the mechanism of action may involve other mechanisms other than inhibition of prostaglandin synthesis.

### Indications and Clinical Uses

Carprofen is used primarily for treatment of musculoskeletal pain and acute pain related to surgery or trauma. It is used primarily for treatment of dogs. Long-term safe use in cats has not been established. However, it is registered in Europe for one-time administration in cats at 4 mg/kg injection. Although use in large animals is uncommon, in cattle, carprofen has been shown to reduce inflammation in cows associated

with *Escherichia coli* mastitis at a dose of 0.7 mg/kg IV. In cattle, carprofen is registered in Europe for treatment of fever associated with mastitis and used to reduce inflammation associated with bovine respiratory disease. Although carprofen has been used in horses, it does not show the same COX-2 selectivity of inhibition as in dogs.

## Precautionary Information

### Adverse Reactions and Side Effects

Safety of carprofen in dogs was determined by the sponsor during preclinical studies. The most common adverse effect in dogs has been in the GI tract (vomiting, anorexia, and diarrhea). Gastrointestinal ulcers, perforation, and bleeding are uncommon in dogs. In rare cases, carprofen has caused idiosyncratic acute hepatic toxicity in dogs. Signs of toxicity usually appear 2-3 weeks after exposure. There were no adverse effects on kidneys when carprofen was evaluated in anesthetized dogs. Carprofen may lower total thyroid ( $T_4$ ) concentrations in dogs but not free  $T_4$ . In experimental dogs, it has inhibited bone healing in some models (4.4 mg/kg per day  $\times$  120 days), but this has not been shown to be a clinical problem. Carprofen has produced toxicity in cats if administered at the same dose rates as for dogs.

### Contraindications and Precautions

Do not use in cats at doses intended for dogs. Do not administer to animals prone to gastrointestinal ulcers. Do not administer with ulcerogenic drugs such as corticosteroids. If a patient has had previous adverse effects from NSAIDs, carprofen should be used cautiously.

### Drug Interactions

Use NSAIDs cautiously with other drugs known to cause gastrointestinal injury (e.g., corticosteroids). The efficacy of ACE inhibitors and diuretics (e.g., furosemide) may be diminished when administered concurrently with NSAIDs.

## Instructions for Use

Doses are based on clinical investigations in dogs with arthritis and for treatment of pain associated with surgery. Dogs may receive carprofen either once daily or twice daily with similar effectiveness and safety. The only approved dose for cats is 4 mg/kg as a one-time injection for surgical pain. However, for long-term use, pharmacokinetic extrapolations suggest a long-term dose of 0.5 mg/kg q24h PO. Long-term safety at this dose has not been established.

## Patient Monitoring and Laboratory Tests

After administration has begun, one should monitor hepatic enzymes for evidence of drug-induced hepatic toxicity approximately 7-14 days after treatment has started. If liver enzymes are elevated, discontinue the medication and contact the drug manufacturer.

## Formulations

- Carprofen is available in 25-, 75-, and 100-mg caplets; 25-, 75- and 100-mg chewable tablets; and injectable solution: 50 mg/mL.
- Zinecarp injection has also been available in Europe.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Carprofen has been compounded by mixing tablets with methylcellulose gel (1%), simple syrup, and a suspending and flavoring vehicle to make a 1.25-, 2.5- and 5-mg/mL suspension. This formulation was stable if stored in the refrigerator or at room temperature for 28 days.

**Small Animal Dosage****Dogs**

- 2.2 mg/kg, q12h PO or 4.4 mg/kg q24h PO.
- 2.2 mg/kg q12h SQ or 4.4 mg/kg q24h SQ.

**Cats**

- 4 mg/kg given once by injection or 0.5 mg/kg q24h PO for long-term use (safety for long-term use has not been established).

**Large Animal Dosage****Horses**

- 0.7 mg/kg q24h IV (in Europe, oral granules: 0.7 mg/kg PO).

**Cattle**

- 1.4 mg/kg SQ, IV.

**Regulatory Information**

Withdrawal times have not been established for carvedilol in the US. It is suggested, based on European labeling, that the withdrawal time for meat is 21 days but zero days for milk. Caution is advised when considering carvedilol for cattle because it has a longer half-life in cows compared to other animals (30-40 hours).

RCI Classification: 4

**Carvedilol**

kar-ved' ih-lole

**Trade and other names:** Coreg

**Functional classification:** Antiarrhythmic

**Pharmacology and Mechanism of Action**

Antiarrhythmic. Nonselective beta-receptor blocker. Carvedilol is a third-generation adrenergic blocker. Carvedilol blocks both  $\beta_1$ -receptors and  $\beta_2$ -receptors in heart and other tissues. Carvedilol is unique because it also has alpha-receptor-blocking properties that will produce vasodilation. It also is reported to have antioxidant properties. It has been shown to prolong survival in human patients with heart failure, but this effect has not been measured in animals.

In dogs the half-life is short (1.2 hrs). Oral absorption is low and variable because of high systemic clearance and first-pass effects. Average oral absorption in one study was only 14% and highly variable, but in another study it was only 1.6% (range 0.4%-54%), making the oral use of carvedilol in dogs unpredictable.

**Indications and Clinical Uses**

Carvedilol has been used to treat arrhythmias in animals. It is also used to treat systemic hypertension and to block beta-cardiac receptors in animals with rapid heart rates. Efficacy has been based on anecdotal accounts, extrapolation from humans, and limited studies in healthy dogs. In healthy dogs, 0.2 mg/kg PO decreased heart rate and 0.4 mg/kg PO decreased heart rate and lowered blood pressure. At 0.4 mg/kg, the effects in healthy dogs persisted for 36 hours. In other studies, doses of 0.3 mg/kg were not effective. In clinical patients, the optimum dose is not known and long-term benefits have not been established. Because oral absorption is inconsistent in dogs (discussed in the pharmacology section), the response may be variable.

Elimination is rapid after oral administration to dogs, but clinical pharmacodynamic effects may persist for up to 12 hours, possibly from the metabolites.

### Precautionary Information

#### Adverse Reactions and Side Effects

Bradycardia can occur resulting from beta-receptor blockade. Carvedilol increases risk of myocardial depression and decreased cardiac output. Adverse effects from nonselective beta-receptor blockade are possible in other tissues. In research dogs administered doses from 0.3 mg/kg to 1.0 mg/kg there was a dose-dependent increase in dizziness, bradycardia, and negative inotropic and chronotropic effects. There was a dose-dependent increase in exercise intolerance at higher doses.

#### Contraindications and Precautions

Use carefully in patients with limited cardiac reserve. Do not administer to dehydrated or hypotensive animals. Use carefully in patients with respiratory disease because the beta<sub>2</sub>-blocking properties can worsen bronchoconstriction.

#### Drug Interactions

Use with other beta blockers will increase its effect. Do not administer with other drugs that may cause hypotension.

### Instructions for Use

Doses in dogs established through clinical experience and limited trials. In a dose titration study in dogs, the effective dose was 0.2-0.4 mg/kg q24h, PO.

### Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and rhythm carefully during treatment. During the initial phase of dosing, monitor patients for worsening of heart failure.

### Formulations

- Carvedilol is available in 3.125-, 6.25-, 12.5-, and 25-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Carvedilol is not soluble in water. Carvedilol compounded suspension has been prepared by adding 25-mg tablets to water to make a paste, then mixed with simple syrup to make a 2-mg/mL or 10-mg/mL suspension for oral administration. This suspension has been stable for 90 days at room temperature, protected from light.

### Small Animal Dosage

#### Dogs

- Initial recommendations published were 0.2 mg/kg q24h PO, followed by gradually increasing the frequency to q12h, and followed by increases up to a maximum of 0.4 mg/kg q12h. More recent evidence suggests a dose of 1.5 mg/kg q12h PO is more effective, but even these doses have not been effective in some dogs.

#### Cats

- Dose not established.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Cascara Sagrada

kass-kar'ah sah-grah'dah

**Trade and other names:** Nature's Remedy and generic brands

**Functional classification:** Laxative

### Pharmacology and Mechanism of Action

Stimulant cathartic. Action is believed to be by local stimulation of bowel motility.

### Indications and Clinical Uses

Laxative used to treat constipation or evacuate bowel for procedures.

#### Precautionary Information

##### Adverse Reactions and Side Effects

Overuse can cause electrolyte losses.

##### Contraindications and Precautions

Do not use in cases where there may be intestinal obstruction.

##### Drug Interactions

No drug interactions are reported in animals.

### Instructions for Use

Available in various dietary supplements.

### Patient Monitoring and Laboratory Tests

Monitor electrolytes with chronic therapy.

### Formulations

- Cascara sagrada is available in a variety of strengths, including tablets, capsules, and liquids.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 1-5 mg/kg/day PO.

#### Cats

- 1-2 mg/cat/day PO.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Do not administer to animals intended for food.

## Castor Oil

kas'tar oil

**Trade and other names:** Generic brands

**Functional classification:** Laxative

## Pharmacology and Mechanism of Action

Stimulant cathartic. Action is believed to be by local stimulation of bowel motility.

## Indications and Clinical Uses

Castor oil is used as a laxative to treat constipation or to evacuate the bowel for procedures.

### Precautionary Information

#### Adverse Reactions and Side Effects

Overuse can cause electrolyte losses. Castor oil has been known to stimulate premature labor in pregnancy.

#### Contraindications and Precautions

Do not use in pregnant animals. It may induce labor. Castor oil has been known to induce histamine release. Monitor patients for signs of histamine reaction.

#### Drug Interactions

No drug interactions are reported in animals.

## Instructions for Use

Use in animals is strictly empirical. It is available as an OTC product. Pet owners should be discouraged from repeated administration to pets.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Castor oil is available in an oral liquid (100%), and 700-mg “Castroclean” capsules.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 8-30 mL/day PO.

### Cats

- 4-10 mL/day PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available.

## Cefaclor

sef 'ah-klor

**Trade and other names:** Generic

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are

divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefaclor, like other second-generation cephalosporins, is more active against gram-negative bacteria and has been used to treat infections caused by bacteria resistant to first-generation drugs.

### Indications and Clinical Uses

Cefaclor is not used commonly in veterinary medicine because other cephalosporins are in more widespread use. However, it may be indicated for treatment of infections caused by bacteria that are resistant to first-generation cephalosporins. Although it has been used as oral therapy, the extent of oral absorption and efficacy information is not available for dogs or cats. Dosing regimens and indications are primarily derived from extrapolation and anecdotal information.

### Precautionary Information

#### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cross-reactivity between penicillin allergy and cephalosporin allergy is low. Rare bleeding disorders have been known to occur with some cephalosporins. Oral administration can potentially produce vomiting and diarrhea in small animals.

#### Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross-sensitivity between penicillins and cephalosporins is small (less than 10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an N-methylthiotetrazole (NMTT) side chain and include cefotetan, cefamandole, and cefoperazone. Oral absorption has not been measured in large animals, and cefaclor is not recommended unless information derived from pharmacokinetic or efficacy studies is available.

#### Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs in a compounded formulation because inactivation may result.

### Instructions for Use

It is used primarily when resistance has been demonstrated to first-generation cephalosporins and other alternatives have been considered.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible bacteria is  $\leq 8$  mcg/mL.

### Formulations

- Cefaclor is available in 250- and 500-mg capsules and 25-, 37.5-, 50-, and 75-mg/mL oral suspension.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 15-20 mg/kg q8h PO.

#### Cats

- 15-20 mg/kg q8h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

## Cefadroxil

sef-ah-drox'il

**Trade and other names:** Cefa-Tabs and Cefa-Drops (veterinary preparations) and Duricef and generic (human preparation)

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefadroxil is a first-generation cephalosporin, and activity and clinical use are similar to cephalexin. Like other first-generation cephalosporins, it is active against *Streptococcus* and *Staphylococcus* species and some gram-negative bacilli, such as *Pasteurella*, *Escherichia coli*, and *Klebsiella pneumoniae*. However, resistance is common among gram-negative bacteria. It is not active against *Pseudomonas aeruginosa*. Methicillin-resistant *Staphylococcus* (MRS) that are resistant to oxacillin will be resistant to first-generation cephalosporins.

## Indications and Clinical Uses

Like other first-generation cephalosporins, it is indicated for treating common infections in animals, including UTIs, skin and soft tissue infections, pyoderma and other dermal infections, and pneumonia. Efficacy against infections caused by anaerobic bacteria is unpredictable. Adequate oral absorption has been shown for foals but not for adult horses.

## Precautionary Information

### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cross-reactivity between penicillin allergy and cephalosporin allergy is low. Rare bleeding disorders have been known to occur with some cephalosporins. Cefadroxil has been known to cause vomiting after oral administration in dogs. Some estimates show that this can occur in up to 10% of treated dogs. If administered orally to adult horses, diarrhea is possible.

### Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (less than 10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an NMTH side chain and include cefotetan, cefamandole, and cefoperazone.



**Drug Interactions**

No drug interactions are reported in animals. However, do not mix with other drugs in a compounded formulation because inactivation may result.

**Instructions for Use**

Spectrum of cefadroxil is similar to other first-generation cephalosporins. The U.S. Food and Drug Administration (FDA)–approved label is appropriate for dosing ranges. For susceptibility test, use cephalothin as test drug.

**Patient Monitoring and Laboratory Tests**

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 2$  mcg/mL for all organisms. Cephalothin is used as a marker to test for sensitivity to cephalexin, cefadroxil, and cephradine.

**Formulations**

- Cefadroxil is available in 50-mg/mL oral suspension and 50-, 100-, 200-, and 1000-mg tablets for veterinary use. However, availability of veterinary-labeled tablets has been inconsistent. It is also available in 500-mg capsules and 25-, 50-, and 100-mg/mL suspension for human use.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Avoid moisture to prevent hydrolysis.

Suspension is stable for 14 days refrigerated and 10 days at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- 22 mg/kg q12h PO, up to 30 mg/kg q12h PO.

**Cats**

- 22 mg/kg q24h PO.

**Large Animal Dosage****Foals**

- 30 mg/kg q12h PO. Note: Oral absorption is adequate only in foals and not in adults or ruminants.

**Regulatory Information**

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

**Cefazolin Sodium**

sef-ah'zoe-lin so'dee-um

**Trade and other names:** Ancef, Kefzol, and generic brands

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibits synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are

divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefazolin is a first-generation cephalosporin. Like other first-generation cephalosporins, it is active against *Streptococcus* and *Staphylococcus* species and some gram-negative bacilli, such as *Pasteurella*, *Escherichia coli*, and *Klebsiella pneumoniae*. The difference between cefazolin and other first-generation cephalosporins is that it is slightly more active against gram-negative *Enterobacteriaceae* and its spectrum resembles some second-generation drugs. Nevertheless, resistance is common among gram-negative bacteria. It is not active against *Pseudomonas aeruginosa*. Methicillin-resistant *Staphylococcus aureus* and other staphylococci resistant to oxacillin will be resistant to first-generation cephalosporins. In dogs, the half-life, clearance, and volume of distribution (V) are 1.04 hours, 2.9 mL/kg/min, and 0.27 L/kg, respectively. These values in horses are 0.62 hours, 5.07 mL/kg/min, and 0.27 L/kg, respectively.

### Indications and Clinical Uses

Cefazolin, because it is injectable, is the most common drug to be administered prophylactically prior to surgery. It is one of the most frequently injected cephalosporin antibiotics used in small animals. Like other first-generation cephalosporins, it is indicated for treating common infections in animals, including UTIs, soft tissue infections, pyoderma and other dermal infections, and pneumonia. Efficacy against infections caused by anaerobic bacteria is unpredictable.

### Precautionary Information

#### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cross-reactivity between penicillin allergy and cephalosporin allergy is low. Rare bleeding disorders have been known to occur with some cephalosporins; however, bleeding problems have not been observed from cefazolin. Some cephalosporins have caused seizures, but this is a rare problem. When administered during surgery, it did not adversely affect cardiovascular function in dogs.

#### Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross-sensitivity between penicillins and cephalosporins is small (less than 10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an NMTH side chain and include cefotetan, cefamandole, and cefoperazone.

#### Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

### Instructions for Use

Cefazolin is a commonly used first-generation cephalosporin as an injectable drug for prophylaxis for surgery and for acute therapy for serious infections. Use cephalothin to test susceptibility, although cefazolin is slightly more active against some gram-negative bacilli.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 2$  mcg/mL for coagulase-positive staphylococci, *Pasteurella multocida*, streptococci beta-hemolytic group, and *E. coli*.

**Formulations**

- Cefazolin is available in 50 and 100 mg/50 mL for injection, in 1 gram or 500 mg vials. Reconstituted to produce 275 or 330 mg/mL.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. If slight yellow discoloration occurs, the solution is still stable. After reconstitution, it is stable for 24 hours at room temperature and 14 days refrigerated. It remains stable if frozen for 3 months.

**Small Animal Dosage****Dogs and Cats**

- 20-35 mg/kg q8h IV or IM.
- Constant-rate infusion (CRI): 1.3 mg/kg loading dose, followed by 1.2 mg/kg/hr.
- Perisurgical use: 22 mg/kg IV every 2 hours during surgery.

**Large Animal Dosage****Horses**

- 25 mg/kg q6-8h IM or IV.

**Regulatory Information**

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

**Cefdinir**

sef 'dih-neer

**Trade and other names:** Omnicef**Functional classification:** Antibacterial**Pharmacology and Mechanism of Action**

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibits synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. It is an oral third-generation cephalosporin and is active against staphylococci and many gram-negative bacilli.

**Indications and Clinical Uses**

Cefdinir is an oral third-generation cephalosporin used in people. Although it has been used as oral therapy, the extent of oral absorption and efficacy information is not available for dogs or cats. Dosing regimens and indications are primarily derived from extrapolation and anecdotal information. It has potential efficacy for infections of the skin, soft tissues, and urinary tract; however, in most instances other cephalosporins such as cefpodoxime proxetil may be substituted instead.

## Precautionary Information

### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. Oral cephalosporins can produce vomiting and diarrhea in small animals.

### Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross-sensitivity between penicillins and cephalosporins is small (less than 10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an NMTT side chain and include cefotetan, cefamandole, and cefoperazone. Oral absorption has not been measured in large animals, and cefdinir is not recommended unless information derived from pharmacokinetic or efficacy studies is available.

### Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs in a compounded formulation because inactivation may result.

## Instructions for Use

Use in veterinary medicine has not been reported. Use and doses are extrapolated from human preparations.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 2$  mcg/mL for all organisms.

## Formulations

- Cefdinir is available in 300-mg capsules and 25-mg/mL oral suspension.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- Dose not established. Human dose is 7 mg/kg q12h PO, and similar doses of 10 mg/kg q12h PO have been used in animals.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

## Cefepime

sef 'ah-peem

**Trade and other names:** Maxipime**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Antibacterial drug of the cephalosporin class. Action against bacterial cell walls is similar to other cephalosporins. Cefepime is one of the fourth-generation cephalosporins. It has an enhanced, extended spectrum that is beyond that of the older cephalosporins. Its activity includes gram-positive cocci and gram-negative bacilli. It has been active against organisms resistant to other beta-lactams such as *Escherichia coli* and *Klebsiella*. It is active against most *Pseudomonas aeruginosa*. It is not active against methicillin-resistant staphylococci, *Bacteroides fragilis*, or penicillin-resistant enterococci.

### Indications and Clinical Uses

Cefepime is a fourth-generation cephalosporin. Although it has a broader spectrum than other cephalosporins, the use has been limited in veterinary medicine. Experimental studies have been conducted in foals, adult horses, and dogs to establish doses, but reports of efficacy are not available.

### Precautionary Information

#### Adverse Reactions and Side Effects

Cefepime is generally safe. However, clinicians should consider the same possible side effects as for other cephalosporins, which include the possibility of bleeding disorders, allergy, vomiting, and diarrhea.

#### Contraindications and Precautions

Do not administer to patients with sensitivity or allergy to cephalosporins. Reduce dose to less frequent intervals (e.g., every 12 hours or every 24 hours) in patients with renal failure.

#### Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

### Instructions for Use

Reconstitute with sterile water, sodium chloride, and 5% dextrose. It may be reconstituted with 1% lidocaine if pain from injection is a problem. Reconstituted solutions are stable for 24 hours at room temperature and 7 days in the refrigerator. Do not mix with other injectable antibiotics. Injection vials also contain L-arginine.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 8$  mcg/mL for all organisms.

### Formulations

- Cefepime is available in 500-mg, 1-g, and 2-g vials for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Observe manufacturer's recommendations for stability after vial is reconstituted.

## Small Animal Dosage

### Dogs

- 40 mg/kg q6h IM or IV.
- CRI: 1.4 mg/kg loading dose, followed by 1.1 mg/kg/hr.

## Large Animal Dosage

### Foals

- 11 mg/kg q8h IV.

## Regulatory Information

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

## Cefixime

sef-iks 'eem

**Trade and other names:** Suprax

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefixime is an oral third-generation cephalosporin, but is not expected to have the same degree of activity against gram-negative bacilli as injectable third-generation cephalosporins such as cefotaxime. Against *Staphylococcus*, cefixime is less active than the oral drug cefpodoxime.

## Indications and Clinical Uses

Cefixime is one of the few oral third-generation cephalosporins. It has been administered orally in dogs and cats to treat infections of the skin, soft tissues, and urinary tract. It is not as active as cefpodoxime against *Staphylococcus*, and because of availability of cefpodoxime for animals, it is substituted instead for most indications.

## Precautionary Information

### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cross-reactivity between penicillin allergy and cephalosporin allergy is low. Rare bleeding disorders have been known to occur with some cephalosporins. Vomiting and diarrhea are possible from oral cephalosporins.

### Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross-sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an NMTT side chain and include cefotetan, cefamandole, and cefoperazone. Oral absorption has not been

measured in large animals, and cefixime is not recommended unless information derived from pharmacokinetic or efficacy studies is available.

### **Drug Interactions**

No drug interactions are reported in animals. However, do not mix with other drugs in a compounded formulation because inactivation may result.

### **Instructions for Use**

Although not approved for veterinary use, pharmacokinetic studies in dogs have provided recommended doses. Note that break point for sensitivity is lower than for other cephalosporins, indicating that organisms tested as susceptible to other cephalosporins may not be susceptible to cefixime.

### **Patient Monitoring and Laboratory Tests**

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 1$  mcg/mL for all organisms.

### **Formulations**

- Cefixime is available in 20- or 40-mg/mL oral suspension and 400-mg tablets.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### **Small Animal Dosage**

#### **Dogs and Cats**

- 10 mg/kg q12h PO.
- Urinary tract infection: 5 mg/kg q12-24h PO.

### **Large Animal Dosage**

- No dose has been reported for large animals.

### **Regulatory Information**

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

## **Cefotaxime Sodium**

sef-oh-taks'eem so'dee-um

**Trade and other names:** Claforan

**Functional classification:** Antibacterial

### **Pharmacology and Mechanism of Action**

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibits synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefotaxime is a third-generation cephalosporin. Like other third-generation cephalosporins, it has enhanced activity against gram-negative bacilli, especially *Enterobacteriaceae*, which may be resistant to first- and second-generation cephalosporins, ampicillin derivatives, and other drugs. It is active against *Escherichia coli*, *Klebsiella*

*pneumoniae*, *Enterobacteriaceae*, *Pasteurella* species, and *Salmonella* species, among others. It is generally not active against *Pseudomonas aeruginosa*. It is active against streptococci, but *Staphylococcus* species are less susceptible. All methicillin-resistant strains of staphylococci will be resistant. Activity against anaerobic bacteria is unpredictable.

### Indications and Clinical Uses

Cefotaxime is used when resistance is encountered to other antibiotics or when infection is in the central nervous system (CNS). Because it is injectable, is expensive, and must be administered frequently, it is not used for routine infections in veterinary medicine when other drugs will be active. Although cefotaxime is not FDA approved for use in animals, it can be legally administered as an extra-label injectable third-generation cephalosporins used in small animals. The use in large animals is uncommon and extra-label administration of cephalosporins is illegal in the United States.

### Precautionary Information

#### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cross-reactivity between penicillin allergy and cephalosporin allergy is low. Rare bleeding disorders have been known to occur with some cephalosporins.

#### Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross-sensitivity between penicillins and cephalosporins is small (less than 10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an NMTT side chain and include cefotetan, cefamandole, and cefoperazone.

#### Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

### Instructions for Use

Third-generation cephalosporin is used when resistance to first- and second-generation cephalosporins is encountered.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 2$  mcg/mL for gram-positive and gram-negative bacteria.

### Formulations

- Cefotaxime is available in 500-mg and 1-, 2-, and 10-g vials for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Maximum stability is at pH of 5-7. Do not mix with alkaline solutions. Yellow or amber color does not indicate instability. After reconstitution, cefotaxime is stable for 12 hours at room temperature; it is stable for 5 days when stored in plastic syringes or a vial if kept in refrigerator. It is stable for 13 weeks if frozen. IV solutions in 1000 mL are stable for 24 hours at room temperature or 5 days in refrigerator. Do not refreeze.



**Small Animal Dosage****Dogs**

- 50 mg/kg q12h IV, IM, or SQ.
- CRI: 3.2 mg/kg loading dose, followed by 5 mg/kg/hr.

**Cats**

- 20-80 mg/kg q6h IV or IM.

**Large Animal Dosage****Foals**

- 40 mg/kg q6h IV, bolus injection over 1 minute, or CRI dose for foals: Loading dose of 4 mg/kg followed by 2.5 mg/kg per hour, IV.

**Horses**

- 25 mg/kg q6h, IV.

**Regulatory Information**

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

**Cefotetan Disodium**

sef 'oh-tee-tan dye-soe' dee-um

**Trade and other names:** Generic

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefotetan has been listed with second-generation cephalosporins, but is more properly considered with the cephamycin group of cephalosporins, which have greater stability against the beta-lactamases of anaerobic bacteria such as those of the Bacteroides group. It is slightly more active (lower minimum inhibitory concentration [MIC] values) compared to ceftiofur against many bacteria.

**Indications and Clinical Uses**

Cefotetan, a second-generation cephalosporin of the cephamycin group, has greater activity against anaerobic bacteria and gram-negative bacilli than other cephalosporins and also has activity against aerobic and facultatively anaerobic gram-negative bacilli. Therefore it has been used to treat infections in dogs and cats in which enteric gram-negative bacilli or anaerobes are suspected, including abdominal infections, soft tissue wounds, and prior to surgery.

**Precautionary Information****Adverse Reactions and Side Effects**

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins.

**Contraindications and Precautions**

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross-sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin

anticoagulants. These cephalosporins are those that have an NMTT side chain and include cefotetan, cefamandole, and cefoperazone.

### Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

### Instructions for Use

Second-generation cephalosporin similar to cefoxitin, but may have longer half-life in dogs.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 8$  mcg/mL for gram-negative and gram-positive organisms.

### Formulations

- Cefotetan is available in 1-, 2-, and 10-g vials for injection. Formulations may no longer be commercially available.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Observe manufacturer's recommendations for stability after vial is reconstituted.

### Small Animal Dosage

#### Dogs and Cats

- 30 mg/kg q8h IV or SQ.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

## Cefovecin

sef-oh-ve'sin

**Trade and other names:** Convenia

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefovecin is considered a third-generation cephalosporin based on structural relationships, but may not have the same activity as other injectable third-generation cephalosporins, such as cefotaxime. Cefovecin has good activity against streptococci, *Staphylococcus* species, and some gram-negative bacilli. Cefovecin is more active against *Staphylococcus pseudintermedius* than *Staph. aureus*. Concentrations are generally not high enough for treating systemic infections caused by Enterobacteriaceae such as

*E. coli*, unless the infection is in the lower urinary tract. Minimum inhibitory concentration values are lower for cefovecin than with first-generation cephalosporins. Some *Enterobacteriaceae* can develop resistance. It is not active against *Pseudomonas aeruginosa*. Methicillin-resistant staphylococci are considered resistant to cefovecin. Activity against anaerobic bacteria is unpredictable. Cefovecin is greater than 99% protein bound in cats and greater than 98% in dogs, which is partly responsible for the long duration. The terminal half-life is approximately 7 days in cats and 5 days in dogs, and effective concentrations can be maintained in the tissue fluid of these species for 14 days.

### Indications and Clinical Uses

Cefovecin is approved for use in dogs and cats. It is approved in the US for skin and soft tissue infections, but also has been used to treat UTIs, for which it is approved in some countries. The efficacy of cefovecin for treating infections in other sites, such as the respiratory tract, bone, and CNS, has not been established. In cats it is approved for treating skin and soft-tissue infections which are caused by highly susceptible bacteria such as strains of *Pasteurella multocida*. Experience is limited to administration of cefovecin in dogs and cats; the use in other species, such as horses, large animals, birds, and reptiles, is not recommended until specific dosing recommendations are published. Protein binding is lower in these species, which causes a much shorter half-life than in dogs or cats.

### Precautionary Information

#### Adverse Reactions and Side Effects

The animal safety studies have produced few serious adverse reactions. In dogs and cats, vomiting and diarrhea have been observed in a dose-related manner. With approved doses, mild gastrointestinal upset may be observed for 2-3 days. Injection-site irritation and transient edema occurred with increasing frequency in a dose-related manner and with repeat injections. The long half-life indicates that drug concentrations will persist in animals for at least 60 days after an injection, but at this time, this has not produced adverse reactions attributed to a long persistence of drug in tissues. Allergic reactions are possible with any cephalosporin, but cross-reactivity between penicillin allergy and cephalosporin allergy is low.

#### Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross-sensitivity between penicillins and cephalosporins is small.

#### Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

### Instructions for Use

The approved label in the US indicates that therapeutic concentrations are maintained for an interval of 7 days in dogs. However, pharmacokinetic studies indicated that drug concentrations persist long enough for a 14-day interval for some indications. In Canada and Europe, the approved label dose is 8 mg/kg SQ, once every 14 days, and efficacy has been demonstrated with a 14-day interval for administration. The injection may be repeated for infections that require longer than 14 days for a cure (e.g., canine pyoderma).

### Patient Monitoring and Laboratory Tests

Susceptibility testing: There is no CLSI-approved break point for susceptibility testing, but a break point of  $\leq 2$  mcg/mL for gram-positive and gram-negative bacteria is suggested.

## Formulations

- Cefovecin is available in 10-mL vials containing 800 mg. When reconstituted, it is 80 mg/mL.

## Stability and Storage

Store in original vial in the refrigerator protected from light. Do not freeze. Once reconstituted, vial should be used within 56 days (the original label had a limitation of 28 days). The reconstituted solution may turn slightly yellow, which does not affect potency.

## Small Animal Dosage

### Dogs and Cats

- 8 mg/kg, SQ, every 14 days. For some indications, injections may be repeated at 7 days.

## Large Animal Dosage

- No dose has been established. It is not recommended for large animal species because of pharmacokinetic differences.

## Regulatory Information

Withdrawal times are not established for animals that produce food, and cefovecin should not be administered to food-producing animals. The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations.

## Cefoxitin sodium

Se fox' i tin soe'dee-um

**Trade and other names:** Mefoxitin, Mefoxin, Cefoxil, and generic

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefotetan has been listed with second-generation cephalosporins, but is more properly considered with the cephamycin group of cephalosporins, which have greater stability against the beta-lactamases of anaerobic bacteria such as those of the *Bacteroides* group. In cats, the half-life is 1.6 hours, the volume of distribution is 0.3 L/kg, and the clearance is 2.3 mL/kg/min. In horses, these values are 0.82 hours, 0.12 L/kg, and 4.3 mL/min/kg, respectively. In dogs, these values are 1.3 hours, 0.16 L/kg, and 3.2 mL/kg/min, respectively.

## Indications and Clinical Uses

Cefoxitin, a cephalosporin of the cephamycin group, has greater activity against anaerobic bacteria and gram-negative bacilli than other cephalosporins. Therefore it has been used to treat infections in dogs and cats in which enteric gram-negative bacilli or anaerobes are suspected, including abdominal infections and soft tissue wounds, and prior to surgery.

## Precautionary Information

### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cross-reactivity between penicillin allergy and cephalosporin allergy is low. Rare bleeding disorders have been known to occur with some cephalosporins. Cefoxitin has been administered to dogs during surgery without adversely affecting their cardiovascular function.

### Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross-sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an NMTT side chain and include cefotetan, cefamandole, and cefoperazone.

### Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

## Instructions for Use

Second-generation cephalosporin is often used when activity against anaerobic bacteria is desired.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 8$  mcg/mL for all organisms. Cefoxitin should not be used to test for methicillin-resistant strains of *Staphylococcus* from animals.

## Formulations

- Cefoxitin is available in 1- and 2-g vials for injection (20 or 40 mg/mL).

## Stability and Storage

Store in a tightly sealed container, in the freezer at  $-25^{\circ}\text{C}$  to  $-10^{\circ}\text{C}$ , unless otherwise instructed by the manufacturer. Thaw at room temperature or in refrigerator to dissolve crystals before administration. Do not heat or place in microwave oven. After thawing, solution is potent for 24 hours at room temperature or for 21 days in refrigerator. Protect from light. Once thawed, do not refreeze.

## Small Animal Dosage

### Dogs and Cats

- 30 mg/kg q6-8h IM or IV. 22 mg/kg IV for presurgical use.

## Large Animal Dosage

### Horses

- 20 mg/kg q4-6h IV or IM.

## Regulatory Information

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

## Cefpodoxime Proxetil

sef-poe-doks'eem prahx 'ih-til

**Trade and other names:** Simplicef (veterinary preparation), Vantin (human preparation), and generic

**Functional classification:** Antibacterial

C

### Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefpodoxime is a third-generation cephalosporin, which indicates greater activity against gram-negative bacilli compared to first-generation cephalosporins. However, cefpodoxime is not as active against many gram-negative bacilli as injectable third-generation cephalosporins such as cefotaxime or ceftazidime. Cefpodoxime has better activity against *Staphylococcus* than other oral third-generation cephalosporins. It is not active against *Enterococcus* spp., methicillin-resistant *Staphylococcus* spp., or *Pseudomonas aeruginosa*. Activity against anaerobic bacteria is unpredictable. It is one of the three currently available third-generation oral cephalosporins. It is combined with proxetil to produce an ester to improve oral absorption. Therefore as the ester, it is actually a prodrug that needs to be converted to the active cefpodoxime. Oral absorption in dogs was reported to be 35%. Half-life is 7.2 hours in horses and 5.7 hours in dogs. Protein binding in dogs is 83%.

### Indications and Clinical Uses

Cefpodoxime is indicated for treatment of skin and other soft tissue infections in dogs caused by susceptible organisms. Efficacy has been established in dogs for treatment of skin and soft tissue infections. Cefpodoxime has greater activity against gram-negative bacilli than first-generation cephalosporins; therefore it may be effective for some gram-negative infections. Although not currently registered for treatment of UTIs, approximately 50% of administered dose is excreted in urine and expected to be active for treating UTIs caused by common pathogens. Although not registered for cats or tested in cats, no adverse effects have been reported from occasional use. However, oral absorption in cats has not been examined.

### Precautionary Information

#### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cross-reactivity between penicillin allergy and cephalosporin allergy is low. Rare bleeding disorders have been known to occur with some cephalosporins. Vomiting and diarrhea can occur from oral administration of cephalosporins but because cefpodoxime proxetil is administered as an inactive pro-drug, the gastrointestinal reactions may be less than other oral cephalosporins.

#### Contraindications and Precautions

This drug is best taken with food to improve oral absorption. Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross-sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals

with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an NMTT side chain and include cefotetan, cefamandole, and cefoperazone.

### **Drug Interactions**

There are no important drug interactions reported for animals, but oral absorption of cefpodoxime in people is inhibited by H<sub>2</sub> blockers (e.g., cimetidine and ranitidine) and antacids, which can decrease oral absorption by 30%. Cephalosporins may be administered with other antibiotics to increase the spectrum of activity and produce a synergistic effect. However, do not mix with other drugs in a compounded formulation because inactivation may result.

### **Instructions for Use**

U.S. Food and Drug Administration approval in dogs includes skin and soft tissue infections. It also has been used for UTIs, and based on spectrum and tissue distribution, it has been used for other infections. There has also been occasional use in cats on an extralabel basis.

### **Patient Monitoring and Laboratory Tests**

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 2$  mcg/mL for all organisms. Strains of *Escherichia coli* and *Klebsiella* that have extended spectrum beta lactamase (ESBL) may be clinically resistant.

### **Formulations**

- Cefpodoxime proxetil is available in 100- and 200-mg tablets and 10- and 20-mg/mL oral suspension (human preparation).

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded tablets has not been evaluated. Avoid exposure to moisture.

### **Small Animal Dosage**

#### **Dogs**

- 5-10 mg/kg q24h PO.

#### **Cats**

- A dose has not been established by the manufacturer for cefpodoxime proxetil. Some veterinarians have extrapolated from the canine dose.

### **Large Animal Dosage**

#### **Horses**

- 10 mg/kg oral q6-12h. The 12-hour interval is appropriate for *Klebsiella*, *Pasteurella*, and streptococci. More frequent intervals may be needed for more resistant organisms.

### **Regulatory Information**

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

## Cefquinome sulfate

Sef' quin ome sul' fate

**Trade and other names:** Cobactan and Cephaguard

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Cefquinome, like other cephalosporins, inhibits synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cefquinome is currently the only fourth-generation cephalosporin approved in any country for use in food animals. In contrast to other cephalosporins, cefquinome is not affected by chromosomal-mediated cephalosporinases of the AmpC type or by plasmid-mediated beta-lactamase from some gram-negative bacilli. Bacteria that produce ESBL and methicillin-resistant *Staphylococcus* species will be resistant.

It is currently licensed in Europe but not the US. Cefquinome has good activity against most gram-negative bacilli, especially Enterobacteriaceae. It has been shown to be active against bovine respiratory pathogens that include *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni*. It also is active against pathogens that cause mastitis in cows, including *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus dysgalactiae*, *Streptococcus agalactiae*, and *Streptococcus uberis*. Activity of cefquinome against equine pathogens includes gram-positive and gram-negative bacteria such as *E. coli*, *Streptococcus equi* subsp. *zooepidemicus*, *Klebsiella pneumoniae*, *Enterobacter* spp., *S. aureus*, *Streptococcus equi* subsp. *equi*, *Clostridium perfringens*, and *Actinobacillus equuli*.

In cattle, cefquinome has a half-life of 2.5 hours and is less than 5% protein bound. Cefquinome is not absorbed after oral administration. In pigs or piglets, the half-life is about 9 hours. Because of low protein binding, cefquinome penetrates into the cerebrospinal fluid (CSF) and the synovial fluid in pigs. In horses, cefquinome has a half-life of 2 hours in adult horses and 1.4 hours in foals with protein binding less than 5%. Absorption from IM injection is almost 100% in adults and 87% in foals. In dogs, cefquinome has a half-life of approximately 1 hour from IM and IV administration, and 0.85 hours from SQ administration, and absorption is complete from SQ and IM injection. Volume of distribution is 0.3 L/kg.

### Indications and Clinical Uses

Cefquinome is used in cattle, pigs, and horses to treat infections caused by susceptible pathogens. It is registered in Europe for treatment of respiratory disease, *E. coli* sepsis in calves, and interdigital necrobacillosis (foot rot) in lactating cows in many countries. Cefquinome ointment has been administered intramammary for treatment of *E. coli* mastitis in dairy cattle. In Europe, it is also registered for treatment of swine respiratory disease, arthritis, meningitis, and dermatitis caused by *Pasteurella multocida*, *Haemophilus parasuis*, *Actinobacillus pleuropneumoniae*, *Streptococcus suis*, *Staphylococcus hyicus*, and other cefquinome-sensitive organisms and mastitis-metritis-agalactia syndrome (MMA) with involvement of *E. coli*, *Staphylococcus* spp., *Streptococcus* spp., and other cefquinome-sensitive organisms. In horses, it is registered for respiratory infection caused by *Streptococcus equi* subsp. *zooepidemicus*, and systemic bacterial infection (sepsis) caused by *E. coli*. There is no use of cefquinome reported for small animals.



## Precautionary Information

### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cefquinome injection SQ may cause some injection-site reactions.

High doses may produce diarrhea in horses, but if doses are maintained within the range listed in the dosing section, it has been safe in most horses.

### Contraindications and Precautions

Do not administer to animals prone to sensitivity to beta-lactams.

### Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

## Instructions for Use

Cefquinome is registered in Europe for treatment of infections in cattle, pigs, and horses. In the US, without FDA approval, the use would be a violation. Cefquinome in cattle can be administered SQ or IM, depending on the formulation. In pigs, it is administered IM. In horses, the solution can be administered IV initially, then switched to IM injections.

## Patient Monitoring and Laboratory Tests

Monitor CBC if high doses are administered for long periods. Susceptibility testing: CLSI guidelines for susceptible bacteria are not available.

## Formulations

- In countries in which cefquinome is available, it is a 7.5% (75-mg/mL) injectable suspension, 2.5% (25-mg/mL) injectable suspension, a powder for reconstitution to be used IV in horses and foals (4.5% or 45 mg/mL in a 30-mL or 100-mL vial), and as an intramammary ointment (75 mg in an 8-g syringe).

## Stability and Storage

After the container is opened, the shelf life is 28 days. For the 4.5% IV solution, the shelf life after reconstitution is 10 days when stored in a refrigerator (2° C-8° C).

## Small Animal Dosage

### Dogs and Cats

- 2 mg/kg IV, IM, SQ, q12h.

## Large Animal Dosage (Based on Registration Label in Europe)

### Cattle

- Bovine respiratory disease (BRD): 2.5 mg/kg, IM, q48h (1 mL of 7.5% suspension per 30 kg).
- Respiratory disease and foot rot: 1 mg/kg (2 mL per 50 kg of 2.5% suspension) IM once daily for 3-5 days.
- Mastitis (*E. coli*) systemic involvement: 1 mg/kg, (2 mL per 50 kg of 2.5% suspension) IM once daily for 2 days.
- Septicemia in calves (*E. coli*): 2 mg/kg (4 mL per 50 kg of 2.5% suspension), IM once daily for 3-5 days.

### Pigs

- Respiratory infections: 2 mg/kg (2 mL of 2.5% suspension) IM in the neck once daily for 2 days.
- Meningitis, arthritis, or dermatitis in piglets: 2 mg/kg (2 mL of 2.5% suspension) once daily IM for 5 days.

**Horses**

- Respiratory infections caused by *Streptococcus equi*: 1 mg/kg (1 mL solution per 45 kg) of solution IV or IM, q24h, for 5-10 days.
- Systemic infection (especially septicemia in foals) caused by *E. coli*: 1 mg/kg (1 mL per 45 kg) IV or IM, q12h, for 6-14 days.

**Regulatory Information**

For ceftquinome suspension, do not use in lactating cattle producing milk for human consumption (during lactation or the dry period). Do not use within 2 months prior to first calving in heifers intended for the production of milk for human consumption. In Europe, the meat withdrawal time is 13 days after 2.5 mg/kg SQ, 5 days after 1 mg/kg IM, and 3 days in pigs. Milk withdrawal time after systemic use is 24 hours. After intramammary administration, the meat withdrawal time is 4 days and the milk discard is 5 days. Ceftquinome is not approved in the United States and the extra-label administration of it to food-producing animals in the United States is a violation of FDA regulations.

**Ceftazidime**

sef-tah' zih-deem

**Trade and other names:** Fortaz, Ceptaz, Tazicef, and Tazidime**Functional classification:** Antibacterial**Pharmacology and Mechanism of Action**

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Ceftazidime is a third-generation cephalosporin. Not all third-generation cephalosporins are equal in activity. Ceftazidime is active against many gram-negative bacilli and more active against *Pseudomonas aeruginosa* than other third-generation cephalosporins. However, it may not be as active against some Enterobacteriaceae as cefotaxime. Ceftazidime pharmacokinetics have been studied in several veterinary species, including dogs, cats, cattle, horses, and exotic animals. In mammals the half-life is short (generally 1-2 hours) and volume of distribution reflects extracellular fluid (0.3-0.4 L/kg).

**Indications and Clinical Uses**

Ceftazidime is a third-generation cephalosporin with activity against many gram-negative bacteria resistant to other drugs. Although it is not an FDA-approved drug for animals, it is used often in zoo, exotic, and companion animals because of its activity against many organisms that are resistant to other drugs. Its activity against *P. aeruginosa* distinguishes it from other cephalosporins. Therefore it has been used to treat infections in dogs and cats in which enteric gram-negative bacilli or *P. aeruginosa* are suspected, including abdominal infections, skin infections, soft tissue wounds, and prior to surgery.

**Precautionary Information****Adverse Reactions and Side Effects**

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cross-reactivity between penicillin allergy and cephalosporin allergy is low. Rare bleeding disorders have been known to occur with some cephalosporins.

**Contraindications and Precautions**

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anticoagulants. These cephalosporins are those that have an NMTT side chain and include cefotetan, cefamandole, and cefoperazone.

**Drug Interactions**

Do not mix in a vial or syringe with other drugs because inactivation may result. In particular, there may be mutual inactivation if mixed with aminoglycosides. If mixed with vancomycin, precipitation may occur.

**Instructions for Use**

Ceftazidime may be reconstituted with 1% lidocaine for IM injection to reduce pain. Ceftazidime contains L-arginine. To make up vials containing sodium carbonate, carbon dioxide will form on reconstitution. Venting may be necessary to release gas. Doses listed for dogs and cats are sufficient for treating infections caused by *P. aeruginosa*.

**Patient Monitoring and Laboratory Tests**

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 8$  mcg/mL for all organisms. Resistance to ceftazidime has been used to test for ESBL-producing strains of *Escherichia coli* or *Klebsiella*.

**Formulations**

- Ceftazidime is available in 0.5-, 1-, 2-, and 6-g vials reconstituted to 280 mg/mL.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Slight discoloration to yellow or amber may occur without losing potency. Do not mix in vial with other drugs, but it may be mixed with IV fluid solutions. After reconstitution, solutions are stable for at least 18 hours at room temperature or 7 days if refrigerated. Solutions may be frozen at 20°C to retain potency for 3 months. Once thawed, it should not be refrozen. Thawed solutions are stable for 8 hours at room temperature and for 4 hours if refrigerated.

**Small Animal Dosage****Dogs and Cats**

- 25-30 mg/kg q8h SQ IM (there may be some pain from SQ and IM injection), or q6h for IV administration.
- Constant IV infusion: Give loading dose of 1.2 mg/kg, followed by 1.56 mg/kg/hr delivered in IV fluids.

**Large Animal Dosage****Horses**

- 20 mg/kg q8h IV or IM.

**Regulatory Information**

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

## Ceftiofur Crystalline-Free Acid

sef' tee-oh-fer

**Trade and other names:** Excede, Naxcel XT

**Functional classification:** Antibacterial

C

### Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Ceftiofur hydrochloride and ceftiofur sodium have similar action and spectrum. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Ceftiofur most closely resembles the activity of a third-generation cephalosporin. It has good activity against most gram-negative bacilli, especially *Enterobacteriaceae*. It has potent activity against bovine and swine respiratory pathogens such as *Mannheimia*, *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Salmonella choleraesuis*, *Haemophilus*, and *Streptococcus*. Ceftiofur has activity against some gram-positive cocci, such as streptococci, but activity against *Staphylococcus* is not as high as other cephalosporins. Ceftiofur is rapidly metabolized after administration to metabolites such as desfuroylceftiofur, which is active against bacteria, except that it is less active against *Staphylococcus* than other cephalosporins and the parent drug ceftiofur.

### Indications and Clinical Uses

Ceftiofur crystalline-free acid is indicated for treatment of swine respiratory disease (SRD) caused by *A. pleuropneumoniae*, *P. multocida*, *S. choleraesuis*, *Haemophilus parasuis*, and *Streptococcus suis*. In cattle, it is used for treatment of BRD caused by *Mannheimia haemolytica*, *P. multocida*, and *Histophilus somni* (formerly *Haemophilus somnus*). It also can be administered to control respiratory disease in cattle at high risk of developing BRD (metaphylaxis) associated with *M. haemolytica*, *P. multocida*, and *H. somnus*. This formulation also is approved for treating foot rot in cattle (interdigital necrobacillosis) caused by *Fusobacterium necrophorum*, *Porphyromonas levii*, and *Bacteriodes melaninogenicus*. It is approved for treatment of acute metritis in dairy cattle via a two-dose regimen. It is approved for treatment and control of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis*, and *Streptococcus suis*. This formulation also is approved for use in horses for treatment of respiratory tract infections caused by susceptible *Streptococcus equi* (*S. zooepidemicus*) after administration of two injections. Ceftiofur hydrochloride and ceftiofur crystalline-free acid have also been administered extralabel intramammary to dairy cattle. However, there are specific products designed for intramammary use (Spectramast).

### Precautionary Information

#### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. For ceftiofur, doses that have exceeded the approved label recommendations have caused bone marrow suppression in dogs. Thrombocytopenia and anemia occurred at doses of 6.6 mg/kg and 11 mg/kg when administered to dogs. High doses have caused diarrhea in horses. Injections of the crystalline-free acid formulation to small animals have caused injection-site lesions in some animals and it is generally not recommended. In some horses, injections of ceftiofur crystalline free acid has caused injection site reactions, consisting of swelling and pain, at the injection site.

**Contraindications and Precautions**

Do not administer this formulation (suspension) IV. Do not administer to animals prone to sensitivity to beta-lactams. Do not administer to animals at doses higher than label indication. In horses do not administer more than 20 mL per injection site. Ceftiofur crystalline-free acid should not be used interchangeably with ceftiofur sodium or ceftiofur hydrochloride without consulting label information for differences in dosing and withdrawal times.

**Drug Interactions**

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

**Instructions for Use**

Dosing information is available for pigs, horses, and cattle; it is not available for other animals. There is no information on the use of ceftiofur crystalline free acid in dogs or cats. When administering to cattle, the dose is 6.6 mg/kg. For SQ injection, the injection should be in the middle third of the posterior aspect of the ear or in the posterior aspect of the ear where it attaches to the head (base of the ear) in beef and non-lactating dairy cattle. For subcutaneous injection in the posterior aspect of the ear where it attaches to the head (base of the ear) in lactating dairy cattle. For horses, administer two IM injections, 4 days apart, at a dose of 6.6 mg/kg. For pigs, administer 5 mg/kg IM in the postauricular region of the neck.

**Patient Monitoring and Laboratory Tests**

Monitor CBC if high doses are administered for long periods. Sensitivity testing: CLSI guidelines for susceptible bacteria indicate that susceptible bacteria have MIC values  $\leq 2$  mcg/mL. (Note that for some cephalosporins used in humans, the MIC values for susceptibility may be  $\leq 8.0$  mcg/mL.)

**Formulations**

- Ceftiofur crystalline-free acid is available in an injectable suspension for cattle at 200 mg/mL ceftiofur equivalents (CE).
- Ceftiofur crystalline-free acid is available in an injectable suspension for pigs at 100 mg/mL CE.

**Stability and Storage**

Store at room temperature. Shake well before administration. Protect from freezing. Contents should be used within 12 weeks after the first dose is removed.

**Small Animal Dosage****Dogs and Cats**

- Dose not established for this product. See [ceftiofur sodium for small animal dosage](#).

**Large Animal Dosage****Cattle**

- 6.6 mg/kg, with a single SQ injection in the middle third of the posterior aspect of the ear.

**Horses and Foals**

- 6.6 mg/kg IM in neck muscle (15 mL per 1000 pounds). Administer a second dose in 4 days. Do not administer more than 20 mL in one site.

**Pigs**

- 5.0 mg/kg IM injection in the postauricular region of the neck.

## Regulatory Information

Pig withdrawal times: 14 days.

Cattle withdrawal time (slaughter): 13 days. A withdrawal period has not been established in preruminating calves. Do not use in calves to be processed for veal. Milk withdrawal: Zero days. The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations.

## Ceftiofur Hydrochloride

sef 'tee-oh-fer hye-droe-klor 'ide

**Trade and other names:** Excenel

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Ceftiofur hydrochloride and ceftiofur sodium have similar action and spectrum. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Ceftiofur most closely resembles the activity of a third-generation cephalosporin. It has good activity against most gram-negative bacilli, especially *Enterobacteriaceae*. It has potent activity against bovine respiratory pathogens such as *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni* (formerly *Haemophilus somnus*). Ceftiofur has activity against some gram-positive cocci, such as streptococci, but activity against *Staphylococcus* is not as high as other cephalosporins. Ceftiofur is rapidly metabolized after administration to metabolites such as desfuroylceftiofur, which is active against bacteria, except that it is less active against *Staphylococcus* than other cephalosporins and the parent drug ceftiofur.

## Indications and Clinical Uses

Ceftiofur hydrochloride is used in cattle and pigs for treatment and control of infections caused by susceptible pathogens. It is registered for treatment of respiratory disease in cattle caused by *Mannheimia*, *P. multocida*, and *H. somni* (formerly *H. somnus*). It is used for interdigital necrobacillosis (foot rot) in cattle caused by *Fusobacterium necrophorum* or *Bacteroides melaninogenicus*. Ceftiofur hydrochloride has been shown to be effective for treatment of acute postpartum metritis in dairy cows when administered at 2.2 mg/kg or for treatment of retained fetal membranes by instilling into the uterus (1 g). Ceftiofur hydrochloride is used for treatment of SRD caused by *Actinobacillus*, *P. multocida*, *Salmonella choleraesuis*, and *Streptococcus suis*. Ceftiofur hydrochloride and ceftiofur crystalline-free acid have also been administered via the intramammary route to dairy cattle. For intramammary use, a specific formulation is recommended (Spectramast DC). Although ceftiofur sodium has been used in horses and dogs to treat infections, there is little experience with administration of ceftiofur hydrochloride in these species.

## Precautionary Information

### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. For ceftiofur, doses that have exceeded the approved label recommendations have caused bone marrow suppression in dogs. Thrombocytopenia and

anemia occurred at doses of 6.6 mg/kg and 11 mg/kg when administered to dogs. High doses have caused diarrhea in horses.

### **Contraindications and Precautions**

Do not administer to animals prone to sensitivity to beta-lactams. Do not administer to animals at high doses. Ceftiofur hydrochloride is a sterile suspension and should not be used interchangeably with ceftiofur sodium, which is a solution.

### **Drug Interactions**

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.

## **Instructions for Use**

Dosing information is not available for species other than pigs and cattle. Dosing in cattle may be extended beyond 3 days if necessary. Alternatively, doses have been administered to cattle for BRD at 2.2 mg/kg at 48-hour intervals. Ceftiofur sodium has been used in horses and dogs, but there is no information available on the use of ceftiofur hydrochloride in these species.

## **Patient Monitoring and Laboratory Tests**

Monitor CBC if high doses are administered for long periods. Susceptibility testing: CLSI guidelines for susceptible bacteria indicate that susceptible bacteria have MIC values  $\leq 2$  mcg/mL. (Note that for some human-labeled cephalosporins, the MIC values for susceptibility may be  $\leq 8.0$  mcg/mL.)

## **Formulations**

- Ceftiofur hydrochloride is available in 50-mg/mL sterile suspension.

## **Stability and Storage**

Store at room temperature. Shake well before administration. Protect from freezing.

## **Small Animal Dosage**

### **Dogs and Cats**

- Dose not established for this product. See [ceftiofur sodium for small animal dose](#).

## **Large Animal Dosage**

### **Cattle**

- 1.1-2.2 mg/kg q24h for 3 days IM or SQ.
- Intravaginal (retained fetal membranes): 1 g ceftiofur diluted in 20 mL sterile water infused in uterus once at 14-20 days after calving.

### **Dairy Cows**

- Treatment of postpartum metritis: 2.2 mg/kg once daily for 5 days SQ or IM.

### **Pigs**

- 3-5 mg/kg q24h for 3 days IM.

## **Regulatory Information**

Cattle withdrawal time: 0 days for milk; 3 days for meat.

Pig withdrawal time: 4 days. The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations.

## Ceftiofur Sodium

Sef' tee-oh-fer soe' dee-um

**Trade and other names:** Naxcel

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Ceftiofur hydrochloride and ceftiofur sodium have similar action and spectrum. Action is similar to other beta-lactam antibiotics, which inhibit synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Ceftiofur most closely resembles the activity of a third-generation cephalosporin. It has good activity against most gram-negative bacilli, especially *Enterobacteriaceae*. It has potent activity against bovine and swine respiratory pathogens such as *Mannheimia*, *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Salmonella choleraesuis*, *Haemophilus*, and *Streptococcus*. Ceftiofur has activity against some gram-positive cocci, such as streptococci, but activity against *Staphylococcus* is not as high as other cephalosporins. Ceftiofur is rapidly metabolized after administration to metabolites such as desfuroylceftiofur, which is active against bacteria, except that it is less active against *Staphylococcus* than other cephalosporins and the parent drug ceftiofur.

### Indications and Clinical Uses

Ceftiofur sodium is used in cattle and pigs for treatment and control of infections caused by susceptible pathogens. It is registered for treatment of respiratory disease and interdigital necrobacillosis (foot rot) in lactating cows in many countries. Ceftiofur has been used for treatment of salmonella in calves. At 5 mg/kg q24h IM, it decreased diarrhea and temperature but did not eradicate the organism. Ceftiofur sodium has been administered on an intramammary basis for treatment of coliform mastitis, but this is an extralabel use. It is used in horses for treatment of streptococcal respiratory infections (registered treatment) and extralabel use for treating other infections such as those caused by gram-negative bacilli, including *Escherichia coli*, *Klebsiella pneumoniae*, and salmonella. Higher doses should be used for nonstreptococcal bacteria in horses. Ceftiofur sodium is registered for a daily SQ injection for treatment of UTIs in dogs, but it has not been evaluated for treatment of other infections.

### Precautionary Information

#### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Rare bleeding disorders have been known to occur with some cephalosporins. For ceftiofur, doses that have exceeded the approved label recommendations have caused bone marrow suppression in dogs. Thrombocytopenia and anemia occurred at doses of 6.6 mg/kg and 11 mg/kg when administered to dogs. High doses have caused diarrhea in horses, but if doses are maintained within the range listed in the dosing section, it has been safe in most horses.

#### Contraindications and Precautions

Do not administer to animals prone to sensitivity to beta-lactams. Do not administer to animals at high doses.

#### Drug Interactions

No drug interactions are reported in animals. However, do not mix in a vial or syringe with other drugs because inactivation may result.



## 142 Ceftriaxone Sodium

### Instructions for Use

Although dosing information is not available for other species, it has been used safely in dogs, sheep, pigs, horses, and cattle and is expected to be safe for other animals. Ceftriaxone sodium is bioequivalent whether administered SQ or IM. In dogs and cats, it has not been evaluated to treat infections other than UTIs in dogs. Higher systemic concentrations may be needed in dogs and cats to treat other infections.

### Patient Monitoring and Laboratory Tests

Monitor CBC if high doses are administered for long periods. Susceptibility testing: CLSI guidelines for susceptible bacteria indicate that susceptible bacteria causing respiratory infections in cattle and pigs have MIC values  $\leq 2$  mcg/mL. The break point for *Streptococcus* in horses is  $\leq 0.25$  mcg/mL. (Note that for many human-labeled cephalosporins, the MIC values for susceptibility may be  $\leq 8.0$  mcg/mL.)

### Formulations

- Ceftriaxone sodium is available in 50-mg/mL vials for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. If not reconstituted, it may be stored at 20-25 degrees C (room temperature). After reconstitution, solutions are potent for 7 days if refrigerated and 12 hours at room temperature. If frozen, solutions are stable for 8 weeks. Do not refreeze. Slight discoloration may occur without losing potency.

### Small Animal Dosage

#### Dogs

- UTI: 2.2-4.4 mg/kg q24h SQ.

#### Cats

- Dose not established, but has been extrapolated from canine dose.

### Large Animal Dosage

#### Horses

- 4.4 mg/kg q24h IM or 2.2 mg/kg q12h IM for as long as 10 days. Treatment of some gram-negative infections may require doses at the higher range, and up to 11 mg/kg/day IM has been given to horses.

#### Foals

- 5 mg/kg q12h IV, or CRI of 1 mg/kg/hour IV.

#### Cattle

- BRD: 1.1-2.2 mg/kg (0.5-1.0 mg/pound) q24h for 3 days IM. Additional doses may be given on days 4 and 5 if necessary. In cattle, these doses also may be administered SQ, which is bioequivalent to other routes of administration.

#### Pigs

- Respiratory infections: 3-5 mg/kg (1.36-2.27 mg/pound) q24h for 3 days IM.

#### Sheep and Goats

- 1.1-2.2 mg/kg (0.5-1.0 mg/pound) q24h for 3 days IM, SQ. Additional doses may be given on days 4 and 5 if necessary.

### Regulatory Information

Cattle withdrawal time: 0 days for milk and 4 days for meat.

Sheep and goat withdrawal time: 0 days for meat.

Pig withdrawal time: 4 days.

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations.

## Cephalexin

sef-ah-lex 'in

**Trade and other names:** Keflex, Rilexine, Vetolexin (Canada), and generic brands. (In European countries it is spelled cephalixin.)

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Cephalosporin antibiotic. Action is similar to other beta-lactam antibiotics, which inhibits synthesis of the bacterial cell wall, leading to cell death. Cephalosporins are divided into first-, second-, third-, and fourth-generation drugs depending on spectrum of activity. Cephalexin is a first-generation cephalosporin. Like other first-generation cephalosporins, it is active against *Streptococcus* and *Staphylococcus* species and some gram-negative bacilli, such as *Pasteurella*, *Escherichia coli*, and *Klebsiella pneumoniae*. However, resistance is common among gram-negative bacteria. It is not active against *Pseudomonas aeruginosa*. *Staphylococcus* spp. resistant to methicillin and oxacillin will be resistant to first-generation cephalosporins.

### Indications and Clinical Uses

Like other first-generation cephalosporins, cephalexin is indicated for treating common infections in animals, including UTIs, soft tissue infections, pyoderma and other dermal infections, and pneumonia. It is approved in the U.S. and other countries for treating skin infections in dogs caused by *Staphylococcus pseudintermedius*. There are published efficacy studies documenting its effectiveness for this indication. Efficacy against infections caused by anaerobic bacteria is unpredictable. In horses, half-life is short at only 1.6 hours and oral absorption is only 5%. In dogs, the oral absorption has ranged from 57% to 90%, depending on the study. In dogs, the half-life, oral clearance, volume of distribution (V/F), and peak concentration ( $C_{MAX}$ ) are 2.74 hours, 3.14 mL/kg/min, 0.92 L/kg, and 19.5 mcg/mL, respectively.

### Precautionary Information

#### Adverse Reactions and Side Effects

All cephalosporins are generally safe; however, sensitivity can occur in individuals (allergy). Cross-reactivity between penicillin allergy and cephalosporin allergy is low. Rare bleeding disorders have been known to occur with some cephalosporins. With oral administration of cephalosporins, vomiting and diarrhea can occur.

#### Contraindications and Precautions

Do not use in animals with allergic sensitivity to other beta-lactams, especially other cephalosporins. However, the incidence of cross-sensitivity between penicillins and cephalosporins is small (<10% in people). Some cephalosporins should not be used in animals with bleeding problems or that are receiving warfarin anti-coagulants. These cephalosporins are those that have an NMTT side chain and include cefotetan, cefamandole, and cefoperazone.

#### Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs in a compounded formulation because inactivation may result.

### Instructions for Use

Although not approved for veterinary use, trials in dogs show efficacy for treating pyoderma. For cephalexin, use cephalothin to test susceptibility.

**Patient Monitoring and Laboratory Tests**

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 2$  mcg/mL for all organisms. Cephalothin is no longer recommended as a marker to test for susceptibility to cephalexin. Cephalexin may be tested primarily in a susceptibility test. Cephalexin may cause a false-positive test for urine glucose. The test may be positive with test strips that use either the copper reduction test or an enzymatic reaction.

**Formulations**

- Cephalexin is available in 250- and 500-mg capsules, 75-, 150-, 300-, and 600-mg chewable tablets (for dogs), 100-mg/mL oral suspension, and 125- and 250-mg/5 mL oral suspension. In Canada a 100 mg- and 250 mg/mL oral paste is available.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Suspensions should be stored in refrigerator and discarded after 14 days. Cephalexin is compatible with enteral products if used immediately after mixing.

**Small Animal Dosage****Dogs**

- Pyoderma and other skin infections: 22-25 mg/kg q12h PO. For other infections: 10-30 mg/kg q6-12h PO.

**Cats**

- 15-20 mg/kg q12h PO.

**Large Animal Dosage****Horses**

- 30 mg/kg q8h PO for susceptible gram-positive bacteria (minimum inhibitory concentration  $\leq 0.5$  mcg/mL).

**Regulatory Information**

The extra-label administration of cephalosporins to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

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**Cetirizine Hydrochloride**

seh-teer 'ih-zeen hye-droe-klor 'ide

**Trade and other names:** Zyrtec

**Functional classification:** Antihistamine

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**Pharmacology and Mechanism of Action**

Antihistamine ( $H_1$ -blocker). Cetirizine is the active metabolite of hydroxyzine. Almost all hydroxyzine in dogs is converted to cetirizine. Cetirizine is similar to other antihistamines—it acts by blocking the histamine type-1 ( $H_1$ ) receptor and suppressing inflammatory reactions caused by histamine. The  $H_1$  blockers have been used to control pruritus and skin inflammation, rhinorrhea, and airway inflammation. Cetirizine is considered a second-generation antihistamine to distinguish it from other older antihistamines. The most important difference between cetirizine and older drugs is that it does not cross the blood-brain barrier as readily and produces less sedation. In cats,

studies have shown cetirizine to be well absorbed after oral administration, with a half-life of 10 hours. In dogs, the half-life is approximately 10-11 hours, and in horses, it is 5.8 hours. A related drug is levocetirizine (Xyzal), which is the active enantiomer of cetirizine and has two-fold higher activity compared to cetirizine.

### Indications and Clinical Uses

Cetirizine is used to treat and prevent allergic reactions in people. It is preferred over older drugs because it has fewer side effects. In dogs and cats, it has been considered for pruritus therapy, allergic airway disease, rhinitis, and other allergic conditions. In cats, 1 mg/kg (5 mg/cat) has produced plasma concentrations considered effective. However, it was not effective in decreasing the inflammatory response in cats with hyperresponsive airways (experimentally induced asthma). In dogs, doses of 2 mg/kg suppress histamine response for 8 hours. However, there are no published clinical trials to document efficacy for these conditions.

### Precautionary Information

#### Adverse Reactions and Side Effects

Sedation is not as likely as with other antihistamines. However, with higher doses, sedation is still possible. Antimuscarinic effects (atropinelike effects) also are possible, but cetirizine may produce fewer antimuscarinic effects than other antihistamines.

#### Contraindications and Precautions

Because antimuscarinic effects (atropinelike effects) are possible, do not use in conditions for which anticholinergic drugs may be contraindicated, such as glaucoma, ileus, or cardiac arrhythmias.

#### Drug Interactions

Do not use with other antimuscarinic drugs.

### Instructions for Use

Use of cetirizine has been mostly empirical. There are no clinical studies to document efficacy.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Cetirizine hydrochloride is available in 1-mg/mL oral syrup and 5- and 10-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 2 mg/kg q12h, PO.

#### Cats

- 1 mg/kg daily, PO.

### Large Animal Dosage

#### Horses

- 0.2-0.4 mg/kg q12h, PO.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Charcoal, Activated

**Trade and other names:** Acta-Char, Charcodote, Liqui-Char, ToxiBan, and generic brands

**Functional classification:** Antidote

### Pharmacology and Mechanism of Action

Adsorbent. It will bind to other drugs and prevent their absorption from the intestine. It may reduce the absorption of a poison by as much as 75%.

### Indications and Clinical Uses

Used primarily to adsorb drugs and toxins in intestine to prevent their absorption. Ordinarily, a single dose is administered, but multiple doses will increase clearance of drugs that may undergo enterohepatic circulation.

#### Precautionary Information

##### Adverse Reactions and Side Effects

Not absorbed systemically. Safe for oral administration, except that constipation may occur; however, formulations that contain sorbitol may induce diarrhea.

##### Contraindications and Precautions

Used primarily as treatment for intoxication.

##### Drug Interactions

Charcoal will adsorb most other drugs administered orally to prevent their absorption.

### Instructions for Use

Dosing of activated charcoal has used a ratio of 10:1 (charcoal:toxin) to administer for treatment of intoxication. However, more recent evidence indicates that a ratio >40:1 is more appropriate, which may require higher doses than previously thought. Activated charcoal is effective to treat intoxication if administered up to 4 hours after exposure, but after 4 hours, benefits decrease. Charcoal is available in a variety of forms and usually is used as treatment for poisoning. Many commercial preparations contain sorbitol, which acts as a flavoring agent and promotes intestinal catharsis.

### Patient Monitoring and Laboratory Tests

When used as treatment for intoxication, careful monitoring of effects of toxin is necessary because charcoal will not adsorb all of the toxicant.

### Formulations

- Charcoal is available in oral suspension and granules. Strengths of formulations vary from 15 g/72 mL to 50/240 mL. Many formulations contain sorbitol, which is a sweetener and also can produce an intestinal cathartic effect.

### Stability and Storage

Store in a tightly sealed container at room temperature. Do not mix with other compounds because it will adsorb other chemicals.

### Small Animal Dosage

#### Dogs and Cats

- 1-4 g/kg PO (granules) or 6-12 mL/kg (suspension). Administer a single dose shortly after poisoning.

## Large Animal Dosage

- Large animal use is not reported, but it may be considered for treatment of a poisoning. Consider a dose of 1 g/kg PO (granules) or 6-10 mL/kg (suspension) PO.

## Regulatory Information

No residue concerns. Withdrawal time: 0 days.

## Chlorambucil

klor-am' byoo-sil

**Trade and other names:** Leukeran

**Functional classification:** Anticancer agent

## Pharmacology and Mechanism of Action

Cytotoxic agent. Chlorambucil is a nitrogen mustard and is sometimes used as a substitute for cyclophosphamide. It has a similar action as cyclophosphamide, but is one of the slowest-acting of the class of nitrogen mustards. When used in metronomic dosing protocols for cancer, it may decrease angiogenesis in tumors.

## Indications and Clinical Uses

Chlorambucil is used for treatment of various tumors and immunosuppressive therapy. Although little has been published on the clinical use of chlorambucil, it may be effective in dogs and cats for immune-mediated disease. However, direct comparisons to other immunosuppressive drugs have not been reported. One of the most frequent uses has been for treatment of immune-mediated skin diseases of cats, for which it has been used to treat cats with pemphigus and eosinophilic granuloma complex (EGC). It also has been used to treat inflammatory bowel disease (IBD) in cats and dogs and has been effective for chronic enteropathy characterized by protein losing enteropathy in dogs.

Chlorambucil also has been used as an anticancer agent in some protocols. It also has been used in metronomic dosing protocols. At a dose of 4 mg/m<sup>2</sup>, PO, every 24 hours, it was well tolerated and produced partial remissions for transitional cell carcinoma.

## Precautionary Information

### Adverse Reactions and Side Effects

Myelosuppression is possible, although most cats tolerate chlorambucil well. Cystitis does not occur with chlorambucil as with cyclophosphamide. Diarrhea and anorexia may occur in some patients. At low doses used in metronomic protocols in dogs, it was well-tolerated.

### Contraindications and Precautions

Cytotoxic, potentially immunosuppressive agent. Do not use in animals with suppressed bone marrow.

### Drug Interactions

Chlorambucil will potentiate other immunosuppressive drugs.

## 148 Chloramphenicol

### Instructions for Use

Chlorambucil may be combined with prednisolone for treatment of immune-mediated disorders. It also can be used in dogs as a continuous treatment (every day dose) at low doses of 4 mg/m<sup>2</sup> every day.

### Patient Monitoring and Laboratory Tests

Monitor CBC in animals during treatment.

### Formulations

- Chlorambucil is available in a 2-mg tablet.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Chlorambucil undergoes rapid hydrolysis (within 10 minutes) in the presence of water. Hydrolysis occurs most readily at pH >2. Therefore chlorambucil can decompose rapidly in compounded aqueous formulations, such as those that contain simple syrup and other excipients. Hydrolysis is slower if mixed in alcohol-based solutions. If mixed with alcohol and stored in the freezer, it is stable for 31 days. Exposure to light reduces the drug's stability.

### Small Animal Dosage

#### Dogs

- 4 mg/m<sup>2</sup> q24h, PO, continuous treatment (metronomic dose protocol). 2-6 mg/m<sup>2</sup> q24h initially, then q48h PO. (Equivalent dose is 0.1-0.2 mg/kg.)
- Intestinal disease: Start with 4-6 mg/m<sup>2</sup>, PO, q24, for first 7-21 days, then reduce dose. It may be administered with prednisolone in refractory cases.

#### Cats

- Immune-mediated disease: 0.1-0.2 mg/kg (approximately one-half tablet) q24h initially, then q48h PO. Often administered concurrently with corticosteroids.
- Inflammatory bowel disease: 2 mg per cat (one tablet), q48-72h, PO.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Chloramphenicol

klor-am fen'ih-kole

**Trade and other names:** Chloramphenicol palmitate, Chloromycetin, chloramphenicol sodium succinate, and generic brands

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Antibacterial drug. Mechanism of action is inhibition of protein synthesis via binding to 50-S ribosome subunit. It has a broad spectrum of activity that includes gram-positive cocci, gram-negative bacilli (including *Enterobacteriaceae*), and Rickettsia. Chloramphenicol is usually regarded as a bacteriostatic drug, and it is important to maintain drug concentrations above the MIC for as long as possible during the

dosing interval. However, there is some evidence that against some bacteria it may have bactericidal effects. Chloramphenicol is well absorbed orally in most animals, except ruminants. The half-life is approximately 2.4 hours in dogs with a volume of distribution (V/F) of 1.6 L/kg and peak concentration of approximately 20 mcg/mL. The half-life is 5 hours in cats but less than 1 hour in horses. After oral administration to foals, however, the half-life is 2.5 hours. The volume of distribution is approximately 1-2 L/kg in most animals. Chloramphenicol sodium succinate is an injectable solution converted to chloramphenicol by hepatic metabolism.

### Indications and Clinical Uses

Antibacterial agent used to treat infections caused by a broad spectrum of organisms, including gram-positive cocci, gram-negative bacilli (including *Enterobacteriaceae*), anaerobic bacteria, and Rickettsia. Chloramphenicol has been used to treat infections caused by bacteria that are resistant to other common drugs (e.g., methicillin-resistant *Staphylococcus* species). Florfenicol acts via a similar mechanism and has been substituted in some animals (see Florfenicol). Chloramphenicol is known for its ability to penetrate lipid membranes and has been used to penetrate tissues with barriers, such as the blood-brain barrier. However, efficacy for treating infections of the CNS has been poor.

### Precautionary Information

#### Adverse Reactions and Side Effects

Chloramphenicol has a narrow margin of safety. High doses can produce toxicity in dogs and cats. Gastrointestinal disturbances are rather common. A decrease in protein synthesis in the bone marrow may be associated with prolonged treatment. The effect on the bone marrow is most prominent in cats, especially after 14 days of treatment, but can occur in any animal when exposure is high. Bone marrow suppression in animals is reversible. Idiosyncratic aplastic anemia has been described in humans. The incidence of aplastic anemia is rare but the consequences are severe because it is irreversible. The risk of human exposure led to the ban of chloramphenicol use in food animals. Another problem recognized in dogs is peripheral neuropathy. This causes ataxia, and weakness, particularly in the hind limbs of dogs. Large breed dogs may be more susceptible to this problem. The peripheral neuropathy is reversible if the drug is discontinued.

#### Contraindications and Precautions

Avoid use in pregnant or neonatal animals. Avoid long-term use in cats. Because exposure in humans can potentially produce severe consequences, veterinarians should caution pet owners about handling the medications, and to ensure that accidental exposure to humans does not occur at home (e.g., to young children). Exposure to small doses has caused aplastic anemia in people.

#### Drug Interactions

Chloramphenicol is notorious for producing drug-drug interactions. Chloramphenicol is a Cytochrome P450 - CYP2B11 inhibitor and possibly other CYP enzymes in dogs. As such, chloramphenicol decreases the clearance of other drugs that are metabolized by the same metabolic enzymes. Chloramphenicol will inhibit the metabolism of opiates, barbiturates, propofol, phenytoin, salicylate, and perhaps other drugs. Therefore, caution should be exercised when administering other drugs metabolized by cytochrome P450 enzymes, particularly anaesthetics, concurrently with chloramphenicol.



## 150 Chlorothiazide

### Instructions for Use

Chloramphenicol use is based on susceptibility data. Although rarely available commercially, chloramphenicol palmitate requires active enzymes and should not be administered to fasted (or anorectic) animals.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 4$  mcg/mL for streptococci and  $\leq 8$  mcg/mL for other organisms.

### Formulations

- Chloramphenicol palmitate is available in a 30-mg/mL oral suspension. Chloramphenicol is available in 250-mg capsules and 100-, 250-, and 500-mg tablets. Chloramphenicol sodium succinate injection, although rarely available, is usually in a concentration of 100 mg/mL (1 gram vial). Some forms of chloramphenicol are no longer available in the US.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Chloramphenicol palmitate is insoluble in water. Chloramphenicol is stable at a pH of 2-7. Chloramphenicol sodium succinate is stable for 30 days at room temperature and 6 months if frozen.

### Small Animal Dosage

#### Chloramphenicol and Chloramphenicol Palmitate

##### Dogs

- 40-50 mg/kg q8h PO.

##### Cats

- 12.5-20 mg/kg q12h PO, (or 50 mg per cat).

#### Chloramphenicol Sodium Succinate

##### Dogs

- 40-50 mg/kg q6-8h IV or IM.

##### Cats

- 12.5-20 mg/cat q12h IV or IM.

### Large Animal Dosage

#### Horses

- 35-50 mg/kg q6-8h PO.

### Regulatory Information

It is illegal to administer chloramphenicol to animals that produce food; therefore no withdrawal times are established.

## Chlorothiazide

klor-oh-thye'ah-zide

**Trade and other names:** Diuril

**Functional classification:** Diuretic

### Pharmacology and Mechanism of Action

Thiazide diuretic. The thiazide diuretics are used infrequently in veterinary medicine. They include hydrochlorothiazide and chlorothiazide. These drugs are sulfonamide analogues and share similar chemical properties, but the pharmacokinetics have not been very well described in animals. The action of thiazides is to inhibit the Na/Cl

cotransporter in the luminal side of the distal tubule. By inhibiting the cotransporter,  $\text{Na}^+$  and  $\text{Cl}^-$  reabsorption is blocked, leading to sodium and water diuresis. Because the action occurs in the distal tubule, these drugs have less of a diuretic effect (less efficacy) than the loop diuretics.

### Indications and Clinical Uses

Chlorothiazide use is not common in animals. There is an approved formulation for dogs (Diuril) but it is not often prescribed. In people, it is used primarily to treat hypertension. In animals, it has been used to treat hypercalciuria (increased calcium in the urine that may lead to urinary calculi). In dairy cattle, it is approved as an oral bolus or injection to treat postparturient udder edema.

Chlorothiazide inhibits sodium reabsorption in distal renal tubules to produce more dilute urine.

Because it decreases renal excretion of calcium, it also has been used to prevent uroliths containing calcium. Dosage regimens used are derived either empirically or from extrapolation of the human dose.

### Precautionary Information

#### Adverse Reactions and Side Effects

Chlorothiazide may cause electrolyte imbalance such as hypokalemia.

#### Contraindications and Precautions

These drugs enhance calcium absorption by decreasing intracellular sodium and enhance the  $\text{Na}^+/\text{Ca}^{++}$  exchange and decrease  $\text{Ca}^{++}$  excretion in urine. They should never be used in hypercalcemia.

#### Drug Interactions

Avoid administering calcium and vitamin D supplements.

### Instructions for Use

Not as effective as high-ceiling diuretics (e.g., furosemide) for producing diuresis.

### Patient Monitoring and Laboratory Tests

Electrolytes should be monitored during chronic therapy.

### Formulations

- Chlorothiazide is available in 250- and 500-mg tablets, 50-mg/mL oral suspension, and injection vials of 500 mg (with mannitol). Cattle formulation: available as 2 gram oral bolus, or 25 mg/mL as a hydrochlorothiazide injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Reconstituted solutions are stable for 24 hours.

### Small Animal Dosage

#### Dogs and Cats

- 20-40 mg/kg q12h PO.

### Large Animal Dosage

#### Cattle

- For treatment of udder edema, 125-250 mg IV or IM injection once or twice per day; or, 2 gram oral bolus once or twice per day.

## Regulatory Information

Withdrawal times: for milk: 72 hours (6 milkings); withdrawal time for meat is not established. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Chlorpheniramine Maleate

klor-fen-eer'ah-meen mal'ee-ate

**Trade and other names:** Chlor-Trimeton and phenetron

**Functional classification:** Antihistamine

## Pharmacology and Mechanism of Action

Antihistamine ( $H_1$ -blocker). Similar to other antihistamines, it acts by blocking the  $H_1$  receptor and suppresses inflammatory reactions caused by histamine. The  $H_1$ -blockers have been used to control pruritus and skin inflammation in dogs and cats. Other commonly used antihistamines include clemastine, chlorpheniramine, diphenhydramine, cetirizine, and hydroxyzine.

## Indications and Clinical Uses

Chlorpheniramine is used to prevent allergic reactions and for pruritus therapy in dogs and cats. However, success rates for treatment of pruritus have not been high. In addition to the antihistamine effect for treating allergies, these drugs block the effect of histamine in the vomiting center, vestibular center, and other centers that control vomiting in animals. Use in animals has been primarily derived from empirical use. There is a lack of well-controlled clinical studies or efficacy trials to document clinical effectiveness.

## Precautionary Information

### Adverse Reactions and Side Effects

Sedation is the most common side effect. It is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to blocking of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors. Antimuscarinic effects (atropinelike effects) also are common, such as dry mouth and decreased gastrointestinal secretions.

### Contraindications and Precautions

Antimuscarinic effects (atropinelike effects) are common. Do not use in conditions for which anticholinergic drugs may be contraindicated, such as glaucoma, ileus, or cardiac arrhythmias.

### Drug Interactions

No drug interactions are reported in animals.

## Instructions for Use

Chlorpheniramine is included as an ingredient in many OTC cough, cold, and allergy medications.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Chlorpheniramine maleate is available in 4- and 8-mg tablets, 2-mg chewable tablets, and 2 mg/5-mL syrup.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Protect from freezing. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 4-8 mg/dog q12h PO; up to a maximum dose of 0.5 mg/kg q12h.

### Cats

- 2 mg/cat q12h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Chlorpromazine

klor-proe'mah-zeen

**Trade and other names:** Thorazine and Largactil

**Functional classification:** Antiemetic, phenothiazine

## Pharmacology and Mechanism of Action

Phenothiazine tranquilizer/antiemetic. Chlorpromazine is a centrally acting dopamine antagonist. It inhibits action of dopamine as a neurotransmitter, which may produce some central-acting effects similar to acepromazine and some antiemetic action.

## Indications and Clinical Uses

Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Chlorpromazine is most often used as a centrally acting antiemetic for disorders that produce vomiting via a central-acting mechanism. It is also used for sedation and preanesthetic purposes, although acepromazine has been much more commonly used.

## Precautionary Information

### Adverse Reactions and Side Effects

Causes sedation. Like acepromazine, it also may cause alpha-adrenergic blockade and vasodilation, but this effect has not been as well documented as for acepromazine. It may produce anticholinergic effects in some animals. Although phenothiazines are reported to decrease the threshold for producing seizures in some animals, this has not been shown in retrospective studies with acepromazine in animals and has not been reported specifically for chlorpromazine. Like other phenothiazines, it may produce extrapyramidal side effects (involuntary muscle

movement) in some individuals. In horses, it has produced undesirable side effects, including violent reactions.

**Contraindications and Precautions**

Use with caution in animals with seizure disorders and animals prone to hypotension. Avoid use in horses.

**Drug Interactions**

It will potentiate effects from other sedatives.

**Instructions for Use**

Chlorpromazine is used for vomiting caused by toxins, drugs, or gastrointestinal disease. Higher doses than listed in dose section have been used with cancer chemotherapy (2 mg/kg q3h SQ).

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Chlorpromazine is available in a 25-mg/mL injection solution, and 10-, 25-, 50-, 100-, and 200-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Slight discoloration does not affect stability. Some sorption (loss) occurs if stored in polyvinyl chloride (soft plastic) containers.

**Small Animal Dosage**

*All Doses Listed Are a One-Time Injection*

**Dogs**

- 0.5 mg/kg q6-8h IM or SQ.

**Cats**

- 0.2-0.4 mg/kg q6-8h, up to 0.5 mg/kg, q8h IM or SQ.

**Large Animal Dosage****Horses**

- Avoid use.

**Cattle**

- 0.22 mg/kg IV or 1.1 mg/kg IM, single dose.

**Sheep and Goats**

- 0.55 mg/kg IV or 2.2 mg/kg IM, single dose.

**Pigs**

- 0.5 mg/kg IM, single dose.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

## Chlortetracycline

klor-tet' rah-sye-kleen

**Trade and other names:** Anaplasmosis block, Aureomycin soluble powder, Aureomycin tablets, Aureomycin soluble calf tablets, Calf Scour Bolus, Fermycin, and generic brands

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Tetracycline antibacterial drug. Inhibits bacterial protein synthesis by interfering with peptide elongation by ribosomes. Chlortetracycline is a bacteriostatic agent with a broad spectrum of activity, which includes gram-positive bacteria and mycoplasma. Most gram-negative bacilli, particularly enteric bacteria (e.g., *Escherichia coli*) of the *Enterobacteriaceae* will be resistant. Chlortetracycline is the least well absorbed of all oral tetracyclines in ruminants and oral administration produces plasma concentrations far below MIC of susceptible bacteria. Therefore, it may be inadequate to treat infections caused by organisms susceptible to tetracyclines.

### Indications and Clinical Uses

Broad-spectrum activity. It is used for routine infections and intracellular pathogens. However, chlortetracycline is poorly absorbed orally and other tetracyclines are preferred for systemic treatment of infections. The most common use for chlortetracycline is as a feed additive to control respiratory and enteric infections in livestock. The clinical use in small animals and horses is rare.

### Precautionary Information

#### Adverse Reactions and Side Effects

Chlortetracycline may bind to bone and developing teeth in young animals. High doses have caused renal injury. Oral administration to horses may produce diarrhea.

#### Contraindications and Precautions

Avoid use in young animals, except where permitted by label for young pigs or cattle.

#### Drug Interactions

Chlortetracycline, like other tetracyclines, will bind to other cations orally administered, which will prevent its absorption. Oral absorption will be decreased if it is administered with products with calcium, zinc, aluminum, magnesium, or iron.

### Instructions for Use

Chlortetracycline is not administered for systemic use in small animals. Doxycycline has replaced most other tetracyclines for treatment in small animals. Most chlortetracycline used is in powdered form and added to feed or drinking water of livestock.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 2$  mcg/mL for streptococci and  $\leq 4$  for other organisms. Tetracycline is used as a marker to test susceptibility for other drugs in this class such as doxycycline, minocycline, and oxytetracycline.

**Formulations**

- Chlortetracycline is available as a powdered feed additive in 25 g/lb or 64 g/lb. It is also available as an anaplasmosis block in 2.5 g/lb and in 25- and 500-mg tablets. (A range of concentrations exists for premix.)

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with ions that may chelate tetracyclines (calcium, magnesium, iron, aluminum, etc.).

**Small Animal Dosage****Dogs and Cats**

- 25 mg/kg q6-8h PO.

**Large Animal Dosage****Cattle**

- Prophylaxis for anaplasmosis: 0.36-0.7 mg/kg/day. (Approximately one block per 10 animals.)
- Tablets: 11 mg/kg q12h for 3-5 days PO.
- Powdered feed additive: 22 mg/kg/day added to water. Actual dose will be affected by feed and water consumption for each animal.

**Pigs**

- Powdered feed additive: 22 mg/kg/day added to water. Actual dose will be affected by feed and water consumption for each animal.

**Regulatory Information**

Cattle withdrawal time for meat: Withdrawal times vary from product to product from 1, 2, 5, or 10 days. Most products list a withdrawal time of 1 day for cattle. Pig withdrawal time for meat: 1-5 days.

Note that for chlortetracycline, withdrawal times may vary considerably from one product to another. One should consult specific product packaging to determine exact withdrawal time.

**Chondroitin Sulfate**

kon-droy'ten sul'fate

**Trade and other names:** Cosequin and Glyco-Flex

**Functional classification:** Nutritional supplement

**Pharmacology and Mechanism of Action**

Nutritional supplement for patients with osteoarthritis. According to the manufacturer, and supported by some experimental evidence, chondroitin sulfate provides precursors to stimulate synthesis of articular cartilage and inhibits degradation and improves healing of articular cartilage.

Pharmacokinetic studies have produced conflicting results depending on formulation, species studied, and assay technique. Although some studies have demonstrated adequate oral absorption, there may be limited oral absorption of the intact large molecule. In dogs, oral absorption has been as low as 5%, but in horses, absorption as high as 22% or 32% has been reported.

It is usually administered in combination with glucosamine. See Glucosamine section for further details.

## Indications and Clinical Uses

Chondroitin sulfate is used primarily for treatment of degenerative joint disease and is usually found in formulations in combination with glucosamine. (See Glucosamine for additional details.) Analyses of published clinical studies in dogs have concluded that there is a moderate level of evidence to indicate some benefit in osteoarthritis, but results may be inconsistent among studies. Benefits of treatment in horses with lameness also have been reported from oral administration of chondroitin–glucosamine supplements.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported, although hypersensitivity is possible. Chondroitin is most often administered with glucosamine. See Glucosamine for potential adverse effects.

#### Contraindications and Precautions

No contraindications have been reported.

#### Drug Interactions

No drug interactions are reported in animals.

## Instructions for Use

Doses are based primarily on empiricism and manufacturer's recommendations. There are limited published trials of efficacy or dose titrations available to determine optimal dose. Doses listed are general recommendations, and products available may vary.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Because several chondroitin sulfate formulations are available, veterinarians are encouraged to carefully examine the product label to ensure proper strength. Veterinary dietary supplements can be highly variable in quality. One product (Cosequin) is available in regular-strength (RS) and double-strength (DS) capsules. Regular-strength capsules contain 250 mg glucosamine, 200 mg chondroitin sulfate and mixed glycosaminoglycans, 5 mg manganese, and 33 mg manganese ascorbate. The DS tablets contain double of each of these amounts.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

*Use the Cosequin RS and DS Strength as a General Guide*

### Dogs

- 1-2 RS capsules per day.
- 2-4 capsules of DS for large dogs.

### Cats

- 1 RS capsule daily.

## Large Animal Dosage

- Horses: 12 mg/kg glucosamine, 3.8 mg/kg chondroitin sulfate twice daily PO for 4 weeks, then 4 mg/kg glucosamine, 1.3 mg/kg chondroitin sulfate thereafter.
- It is common to initiate treatment in horses with a higher dose of 22 mg/kg glucosamine, 8.8 mg/kg chondroitin sulfate, daily PO.



**Regulatory Information**

Withdrawal times are not established for animals that produce food. Chondroitin sulfate and glucosamine are found naturally, and withdrawal times may not be necessary if these supplements are administered to food animals. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Cimetidine Hydrochloride**

sy-met'ih-deen hye-droe-klor'ide

**Trade and other names:** Tagamet (OTC and prescription)

**Functional classification:** Antiulcer agent

**Pharmacology and Mechanism of Action**

Histamine<sub>2</sub> antagonist (H<sub>2</sub> blocker). Stimulation of acid secretion in the stomach requires activation of histamine type 2 receptors, gastrin receptors, and muscarinic receptors. Cimetidine and related H<sub>2</sub> blockers inhibit the action of histamine on the histamine H<sub>2</sub> receptor of parietal cells and inhibit parietal cell gastric acid secretion. Cimetidine increases stomach pH to help heal and prevent gastric and duodenal ulcers. In dogs the half-life is short (1.7 hours) necessitating frequent administration.

**Indications and Clinical Uses**

Cimetidine is used to treat gastric ulcers and gastritis. Although it is often used for animals with vomiting, there are no efficacy data to indicate that it is effective. There also are no efficacy data to support its use for preventing NSAID-induced bleeding and ulcers. In dogs, clinical efficacy is limited and other drugs (e.g., famotidine, ranitidine, and proton pump inhibitors) are preferred for ulcer treatment. In horses, cimetidine has been used to prevent or treat gastrointestinal ulcers. However, the efficacy for these indications has not been proved. For example, studies in horses showed that at 18 g/kg q8h PO, it did not cause healing of ulcers. The poor efficacy may be because of short duration of effect (2-6 hours). In horses, other drugs (e.g., ranitidine and proton pump inhibitors) are preferred for ulcer treatment. In calves, cimetidine will increase abomasal pH.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are usually seen only with decreased renal clearance. In people, CNS signs may occur with high doses.

**Contraindications and Precautions**

Use cautiously with drugs that rely on hepatic metabolism for clearance.

**Drug Interactions**

Cimetidine is a well-known cytochrome P450 enzyme inhibitor. It may increase concentrations of other drugs used concurrently (e.g., theophylline) because of inhibition of hepatic enzymes. Cimetidine will increase the pH of the stomach, which can inhibit oral absorption of some drugs (e.g., itraconazole and ketoconazole). Cimetidine will inhibit the oral absorption of iron supplements.

**Instructions for Use**

Efficacy for treating ulcers in animals has not been established. Frequent dosing may be necessary for suppression of stomach acid. Doses are derived from gastric secretory studies in experimental animals.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Cimetidine is available in 100-, 150-, 200-, 300-, 400-, and 800-mg tablets; a 60-mg/mL oral solution; and a 150-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not store injection formulation in refrigerator. Solutions are stable for at least 14 days. Stable if mixed with various enteral products.

## Small Animal Dosage

### Dogs and Cats

- 10 mg/kg q6-8h IV, IM, or PO.
- Renal failure: 2.5-5 mg/kg q12h IV or PO.

## Large Animal Dosage

### Horses

- 3 mg/kg diluted in fluid solution and infused IV over 2 minutes, q8h.
- 40-60 mg/kg/day PO. However, oral doses in horses produce inconsistent results.

### Calves

- Abomasal ulcers in milk-fed calves: 100 mg/kg q8h PO.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 5

## Ciprofloxacin Hydrochloride

sip-roe-floks'ah-sin hye-droe-klor'ide

**Trade and other names:** Cipro and generic brands

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Fluoroquinolone antibacterial. Ciprofloxacin acts to inhibit DNA gyrase and cell DNA and RNA synthesis. Bactericidal. Broad antimicrobial activity. Ciprofloxacin is active against gram-negative bacilli, including *Enterobacteriaceae* and some gram-positive cocci, including *Staphylococcus*. Ciprofloxacin is more active against *Pseudomonas aeruginosa* than other fluoroquinolones, but resistance is possible. Multiresistant bacteria, including gram-negative bacilli of the *Enterobacteriaceae*, and methicillin-resistant strains of *Staphylococcus*, are likely to be resistant to ciprofloxacin and other fluoroquinolones. Oral absorption of ciprofloxacin in dogs has been variable. Oral absorption may approach 74% to 97%, but has been as low as 42%. In research dogs the oral absorption was 58.4%, but with high variability. In research dogs at a dose of approximately 25 mg/kg PO, the peak plasma concentration was 4.4 mcg/mL, terminal half-life was 2.6 hours, and AUC 22.5 mcg·hr/mL. In a population pharmacokinetic study

(patient population) the half-life was 4.3 hours, and the peak concentration was 1.2 mcg/mL, and AUC was 13.8 mcg hr/mL at an oral dose of 23 mg/kg. Oral absorption in horses is less than 10% and should not be used orally in horses. In cats, oral absorption is low (22%-33%) and would not be effective for gram-positive bacteria even at 10 mg/kg; but at 10 mg/kg q12h, it was able to reach therapeutic targets against susceptible gram-negative bacteria. Other fluoroquinolones registered for animals have near-complete bioavailability.

### **Indications and Clinical Uses**

Ciprofloxacin, although a human drug, has been used in small animals for treatment of a wide variety of infections, including skin infections, pneumonia, and soft tissue infections. Ciprofloxacin is not approved for animals. However, it can be prescribed by veterinarians, as long as it is not administered to animals that produce food or are intended for food. The administration of ciprofloxacin to animals is considered extralabel and subject to other extralabel restrictions. The variable and potentially low ciprofloxacin oral availability for dogs and cats suggests that doses should be higher than the doses currently used for drugs such as enrofloxacin, marbofloxacin, or orbifloxacin. If administered at an oral dose of 25 mg/kg once daily to dogs, the breakpoint for human susceptibility testing will not apply and bacteria should be considered susceptible only if the MIC is less than 0.12 mcg/mL.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

High concentrations may cause CNS toxicity, especially in animals with renal failure. Ciprofloxacin causes occasional vomiting. Intravenous solution should be given slowly (over 30 minutes). At high doses, it may cause some nausea, vomiting, and diarrhea. Blindness in cats has not been reported for ciprofloxacin. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most susceptible to quinolone-induced arthropathy in the age group of 4 weeks to 28 weeks of age. Large, rapidly growing dogs are the most susceptible. Administration to horses may cause severe enteritis and colic.

Intravenous infusions have elicited an anaphylactoid reaction in some dogs. Dogs sensitive to this reactions have shown evidence of hypotension, and cardiac abnormalities, including arrhythmia. Observe dogs for signs of reactions during intravenous infusions.

#### **Contraindications and Precautions**

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures, such as epileptics. It is not recommended to administer ciprofloxacin to horses.

#### **Drug Interactions**

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

### **Instructions for Use**

Doses are based on plasma concentrations needed to achieve sufficient plasma concentration above MIC. Efficacy studies have not been performed in dogs or cats, and clinical use is based primarily on anecdotal experience. Injectable ciprofloxacin is available in a human preparation, usually 10 mg/mL (in sterile water) or 2 mg/mL (premixed

with 5% dextrose). Dilute the concentrated form to 1-2 mg/mL prior to IV use with an IV solution and infuse slowly. Do not infuse concurrently with other medications (e.g., in a piggyback) because inactivation may occur.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms has not been determined for animals, but for humans is  $\leq 1.0$  mcg/mL. The human breakpoint for susceptibility should not be applied to dogs and cats. In dogs, at a dose of 25 mg/kg per day, PO, the cutoff for susceptible bacteria is  $\leq 0.06$  mcg/mL. Most susceptible gram-negative bacteria of the *Enterobacteriaceae* have MIC values less than 0.12 mcg/mL, but the MIC for *Pseudomonas aeruginosa* is typically higher ( $< 0.5$  mcg/mL). *Staphylococcus* spp. typically have MIC values  $< 1.0$  mcg/mL.

### Formulations Available

Ciprofloxacin is available in 100-, 250-, 500-, and 750-mg tablets and 5-, 10-, and 20-mg/mL injection, and 2-mg/mL infusion (in dextrose).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Aqueous solutions of 0.5 to 2 mg/mL retain potency up to 14 days when stored. Do not mix with products that contain ions (e.g., iron, aluminum, magnesium, and calcium).

### Small Animal Dosage

#### Dogs

- 25 mg/kg q24h PO.
- 15 mg/kg q24h IV.

#### Cats

- 20 mg/kg q24h, PO.
- 10 mg/kg q24h IV.

### Large Animal Dosage

- No dosing data available. Ciprofloxacin has poor oral absorption in horses ( $< 10\%$ ) and is not recommended.

### Regulatory Information

There are no withdrawal times established because this drug should not be administered to animals that produce food. The extra-label administration of fluoroquinolones to food-producing animals in the United States is a violation of FDA regulations. Withdrawal times are not established for animals that produce food.

## Cisapride

Siss'ah-pride

**Trade and other names:** Propulsid (Prepulsid in Canada), not currently available commercially

**Functional classification:** Prokinetic agent

### Pharmacology and Mechanism of Action

Prokinetic agent. Its mechanism is believed to be as an agonist for the 5-hydroxytryptamine (5-HT<sub>4</sub>) receptor on myenteric neurons (5-HT<sub>4</sub> ordinarily stimulates cholinergic transmission in the myenteric neurons). It also acts as an antagonist for the 5-HT<sub>3</sub> receptor. Via this mechanism, or independently, cisapride may enhance release of acetylcholine at the myenteric plexus. Cisapride increases the motility of the stomach, small intestine, and colon. It accelerates the transit of contents in the bowel and intestines.

## Indications and Clinical Uses

Cisapride is used to stimulate motility for treating gastric reflux, gastroparesis, ileus, and constipation. The most common uses in animals have been to prevent stomach regurgitation, decrease postoperative ileus, and treat constipation and megacolon in cats. In dogs it was shown to be more effective than other treatments for preventing gastroesophageal reflux in anesthetized dogs. It is not effective to stimulate motility in dogs with megaesophagus. Cisapride was removed from the human market and is no longer commercially available. Compounding pharmacies have made cisapride available to veterinarians in compounded forms (see [Formulations](#) section). However, these formulations are not licensed and are unregulated.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse cardiac effects have been reported in people and are the cause for discontinuation in human medicine. These cardiac effects have not been reported in animals. High overdoses in dogs (18 mg/kg) have produced abdominal pain, aggression, ataxia, fever, and vomiting. With higher overdoses, diarrhea, ataxia, and CNS reactions have been observed.

### Contraindications and Precautions

Contraindicated in patients with gastrointestinal obstruction.

### Drug Interactions

Anticholinergic drugs, such as atropine, will diminish the action. Cisapride should not be used with drugs that inhibit metabolism (cytochrome P450 inhibitors) or drugs that inhibit P-glycoprotein. Toxicity may result (see list of drugs in Appendix).

## Instructions for Use

Not currently available commercially. Cisapride was discontinued by the manufacturer in July 2000. However, some veterinary pharmacies can fill some orders or prepare compounded formulations for animals. Consult local compounding pharmacist about availability. Doses are based on extrapolation from human doses, experimental studies, and anecdotal evidence. Efficacy studies have not been performed in dogs or cats.

## Patient Monitoring and Laboratory Tests

In humans, cardiac effects have been reported (arrhythmias). Monitor electrocardiogram (ECG) in susceptible patients.

## Formulations

- Cisapride was once available in a 10-mg tablet but has been discontinued by the manufacturer. Formulations used are prepared by compounding from a pure source. To prepare 1 mg/mL injectable solution (follow United States Pharmacopeia [USP] <797> sterile compounding standards), mix 0.104 g of cisapride monohydrate with 20 mL tartaric acid 6% solution. Add sterile water to make up a 100-mL total volume. Keep the solution in the refrigerator, in a sterile vial, protected from light, and labeled with Beyond Use Date of 14 days postcompounding. A 10-mg/mL oral suspension (follow USP <795> compounding standards) has been prepared by mixing 300 mg (0.3 g) of cisapride monohydrate with 15 mL Ora Plus and enough Ora Sweet added to make a total of volume of 30 mL (Oral Plus and Ora Sweet are oral formulation suspending agents and vehicles commonly used in commercial pharmacies.)

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Some compounded formulations have been stable for 60 days if the pH is kept neutral. Injectable solution should be used within 14 days. An oral suspension of 10 mg/mL in aqueous vehicle was stable for 30 days in refrigerator.

## Small Animal Dosage

### Dogs

- 0.1-0.5 mg/kg q8-12h PO (up to 0.5-1.0 mg/kg). 1 mg/kg IV if used to prevent gastroesophageal reflux during anesthesia.

### Cats

- 2.5-5 mg/cat q8-12h PO (up to 1 mg/kg q8h).

## Large Animal Dosage

### Horses

- 0.1 mg/kg IV. (This formulation is not commercially available, but an IV form has been made by combining 40 mg with 1.0 mL of tartaric acid and diluted to obtain a total volume of 10 mL.)

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it poses a risk to humans.

## Cisplatin

sis-plah'tin

**Trade and other names:** Platinol

**Functional classification:** Anticancer agent

## Pharmacology and Mechanism of Action

Anticancer agent. Cisplatin acts like a bifunctional alkylator of DNA but forms a reactive carbonium ion, and the cross-linking occurs around the platinum ion instead of an alkyl group. It preferentially binds to the N-7 of guanine and adenine bases. As a result of this reaction, interstrand and intrastrand cross-linking of DNA occurs. The result is inhibition of DNA synthesis. A related drug is carboplatin, which is a second-generation platinum compound used in patients who may not tolerate cisplatin.

## Indications and Clinical Uses

Cisplatin is used for treating various solid tumors, including bronchiogenic carcinoma, osteosarcoma, transitional cell carcinoma, and mast cell tumors. It has been shown to be effective for increasing the survival of dogs that have undergone amputations for osteosarcoma.

## Precautionary Information

### Adverse Reactions and Side Effects

Nephrotoxicity is the most limiting factor to cisplatin therapy. In cats, it causes a dose-related, species-specific, primary pulmonary toxicosis. Vomiting is common in dogs with administration. Transient thrombocytopenia may occur in dogs. Cisplatin has caused potassium wasting and depletion of magnesium.

**Contraindications and Precautions**

Do not use in cats.

**Drug Interactions**

Cisplatin may be used with other cancer chemotherapy agents. Do not use with other nephrotoxic drugs.

**Instructions for Use**

To avoid toxicity, fluid loading before administration using sodium chloride should be performed. Antiemetic agents are often administered before therapy to decrease vomiting. For transitional cell and squamous cell carcinomas, doses used are 40 to 50 mg/m<sup>2</sup> every 21 to 28 days. For osteosarcoma, it has been used at a dose of 70 mg/m<sup>2</sup> every 21 days for four treatments.

**Patient Monitoring and Laboratory Tests**

Monitor renal function in treated animals. Monitor CBC in patients between treatments.

**Formulations**

- Cisplatin is available in a 1-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs**

- 60-70 mg/m<sup>2</sup> q3-4wks IV (administer fluid for diuresis with therapy).

**Cats**

- Do not use in cats.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

**Clarithromycin**

klah-rith'roe-mye'sin

**Trade and other names:** Biaxin and generic brands

**Functional classification:** Antibiotic

**Pharmacology and Mechanism of Action**

Macrolide antibiotic with bacteriostatic activity. It is a substituted 14-carbon macrolide. Clarithromycin was introduced in 1990 as a substitute for erythromycin. Compared with erythromycin, it has higher absorption, a longer half-life, and increased intracellular uptake. Site of action is similar to other macrolide antibiotics, which is the 50-S ribosomal subunit in susceptible bacteria. Spectrum includes primarily gram-positive bacteria. Resistance is expected for most gram-negative bacteria. Clarithromycin may have higher activity (lower MIC values) for many bacteria compared

with erythromycin or azithromycin. Clarithromycin, like other macrolides, may have anti-inflammatory properties that are independent of the microbiologic effects (e.g., inhibit neutrophil and eosinophil inflammatory reaction). Clarithromycin metabolites may contribute to the activity, but these metabolites are not well characterized in animals. It is widely distributed to intracellular and tissue sites with concentrations in most tissues—including the respiratory tract—exceeding the plasma concentration. In foals, half-life is 4.8–5.4 hours with a volume of distribution of 10.5 L/kg and clearance of 1.27 L/kg/hr. The oral absorption in foals is 57% with a maximum concentration of 0.5–0.9 mcg/mL.

## Indications and Clinical Uses

Most common use in people is for treatment of *Helicobacter gastritis* and respiratory infections, where it has retained activity against most respiratory tract pathogens (e.g., *Streptococcus*, mycoplasma, chlamydia). In small animals, clarithromycin has been used for indications such as skin infections and respiratory infections. In foals, clarithromycin has been used for treatment of infections caused by *Rhodococcus equi* (in combination with rifampin) and produced better clinical success than azithromycin.

## Precautionary Information

### Adverse Reactions and Side Effects

The most common adverse effects from clarithromycin and related drugs are diarrhea and nausea. Many animals may develop soft feces or mild diarrhea. In studies in healthy foals, diarrhea was uncommon from oral doses and was self-limiting. However, if diarrhea becomes severe, treatment should be discontinued.

### Contraindications and Precautions

Administer with caution to adult horses, ruminants, rodents, and rabbits because diarrhea and enteritis may develop. Use with caution in pregnant animals.

### Drug Interactions

Many macrolide antibiotics are cytochrome P450 enzyme inhibitors and can decrease metabolism of other drugs. For example, in people, it increased digoxin concentrations. Clarithromycin administered to animals may decrease the clearance of other co-administered drugs. For example, clarithromycin decreased clearance of cyclosporine and increased oral absorption of cyclosporine in cats.

## Instructions for Use

Clarithromycin should be given twice daily to animals because of a short half-life and need for a long time above the MIC.

## Patient Monitoring and Laboratory Tests

In the absence of a specific value for clarithromycin, use susceptibility for erythromycin to guide use of clarithromycin. Although the CLSI-derived break point for susceptible bacteria is 1 mcg/mL, cures have been observed when treating respiratory pathogens with MIC values as high as 8 mcg/mL, which is attributed to high respiratory concentrations achieved. Minimum inhibitory concentration values for *R. equi* were 0.12 mcg/mL. Organisms resistant to erythromycin and azithromycin will most likely be resistant to clarithromycin.

## Formulations

- Clarithromycin is available in 250- and 500-mg tablets and 25- and 50-mg/mL oral suspension.



**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. 250-mg tablets have been dissolved in water (50 mL) and administered immediately to foals orally. However, the long-term stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs and Cats**

- 7.5 mg/kg q12h PO.

**Large Animal Dosage****Foals**

- 7.5 mg/kg q12h PO (often combined with rifampin at 10 mg/kg q12h).

**Pigs**

- 7.5 mg/kg PO, q12h.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Clemastine Fumarate**

Klem'ass-teen fyoo'mar-ate

**Trade and other names:** Tavist and generic brands

**Functional classification:** Antihistamine

**Pharmacology and Mechanism of Action**

Antihistamine ( $H_1$ -blocker). Similar to other antihistamines, it acts by blocking the  $H_1$  receptor and suppresses inflammatory reactions caused by histamine. The  $H_1$ -blockers have been used to control pruritus and skin inflammation in dogs and cats; however, success rates in dogs have not been high. Commonly used antihistamines include clemastine, chlorpheniramine, diphenhydramine, and hydroxyzine.

**Indications and Clinical Uses**

Used primarily for treatment of allergy. Some reports have suggested that clemastine is effective for pruritus in dogs. However, the half-life in dogs is short (3.8 hours), and it has rapid clearance. After oral administration, the oral absorption is only 3% (20%-70% in humans). At a high dose of 0.5 mg/kg PO, it did not suppress intradermal skin reactions. This evidence suggests that oral administration may not be as effective in dogs as previously thought. Oral absorption studies in horses indicated that it is not absorbed when given orally (bioavailability was only 3%).

**Precautionary Information****Adverse Reactions and Side Effects**

Sedation is the most common side effect. Sedation is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to blocking of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors. Antimuscarinic effects (atropinelike effects) also are possible, such as dry mouth and decreased gastrointestinal secretions.

**Contraindications and Precautions**

No contraindications reported for animals.

**Drug Interactions**

No drug interactions are reported in animals.

**Instructions for Use**

Clemastine fumarate is used for short-term treatment of pruritus in dogs. It may be more efficacious when combined with other anti-inflammatory drugs. Tavist syrup contains 5.5% alcohol.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Clemastine fumarate is available in 1.34-mg tablets (OTC), 2.64-mg tablets (prescription), and 0.1-mg/mL syrup.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- 0.05-0.1 mg/kg q12h PO, up to 0.5-1.5 mg/kg q12h PO.
- Dogs < 10 kg in weight: half of tablet. (Dose based on q12h treatment and 1.34-mg tablet.)
- Dogs 10-25 kg in weight: 1 tablet. (Dose based on q12h treatment and 1.34-mg tablets.)
- Dogs >25 kg: 1.5 tablets. (Dose based on q12h treatment and 1.34-mg tablets.)
- mg/kg IV.

**Large Animal Dosage****Horses**

- 50 mcg/kg (0.05 mg/kg) q8h IV. It is not absorbed orally in horses.

**Regulatory Information**

Do not administer to animals that produce food.

RCI Classification: 3

**Clenbuterol**

klen-byoo'ter-ole

**Trade and other names:** Ventipulmin

**Functional classification:** Bronchodilator, beta agonist

**Pharmacology and Mechanism of Action**

Beta<sub>2</sub>-adrenergic agonist (beta<sub>2</sub>/beta<sub>1</sub> ratio = 4.0). Bronchodilator. Stimulates beta<sub>2</sub> receptors to relax bronchial smooth muscle. It also may inhibit release of inflammatory mediators, especially from mast cells, decrease mucus production by goblet cells, and may increase rate of mucociliary transport in the airways. Compared to terbutaline, it has lower efficacy because of lower intrinsic activity, and it is only a partial

agonist. Clenbuterol differs from other beta-agonists because it resists O-sulfate ester conjugation, which produces a longer half-life. It also has better oral absorption (83%) than other beta-agonists in horses. In horses, the plasma half-life is 13 hours, but in urine it can be detected for 12 days. In addition to the effects on respiratory smooth muscle, clenbuterol can produce repartitioning effects, which indicates that it will stimulate development of more muscle (anabolic effect) and less fat (lipolytic effect). The repartitioning effect is caused by leptin- and adiponectin-mediated repartitioning effects that produce an increase in muscle mass. In horses, it decreases the percent body fat and increases muscle mass. The increased muscle mass does not enhance athletic performance, and may actually have a negative effect on athletic performance. Nevertheless, because of the effects on muscle, it has been abused in humans (e.g., bodybuilders) and used illegally for weight gain in food-producing animals.

### **Indications and Clinical Uses**

Clenbuterol is indicated for treatment of animals with reversible bronchoconstriction such as horses with recurrent airway obstruction (RAO), formerly called chronic obstructive pulmonary disease (COPD). The response for treating RAO can be variable. Some horses that do not respond to a low dose respond better at 4x the starting dose with a better response rate. At high doses, tachyphylaxis may occur with repeated high doses. Studies have demonstrated effects in horses, but there are no reports of use in other species. In horses, it can have repartitioning effects (producing less fat), but it has also decreased exercise capacity and increased rate of fatigue. It should not be used in animals intended for food.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Clenbuterol may produce excessive beta-adrenergic stimulation at high doses (tachycardia and tremors). Arrhythmias occur at high doses. Chronic use may have adverse effects on cardiac function in healthy horses. There have been conflicting studies on the effects of clenbuterol on athletic performance of horses. In one study at approved doses it did not have any adverse effects on equine cardiac or skeletal muscle. In other studies it had negative effects on aerobic athletic performance, faster time to fatigue, decreased cardiac function, and decreased oxygen consumption. The negative effects may occur because after repeated doses it down-regulates the adrenergic beta-2 receptor and results in decrease in receptor expression in skeletal muscle and lungs.

#### **Contraindications and Precautions**

Do not administer to animals intended for food. Veterinarians should be warned that clenbuterol is abused in humans for the purpose of muscle building and weight loss. Subsequently, high doses in humans may cause cardiac toxicity, such as arrhythmias.

#### **Drug Interactions**

Because clenbuterol is a beta-agonist, other adrenergic drugs will potentiate the action. In addition, beta-blocking drugs will decrease action. Use with caution with any other drug that may stimulate the heart.

### **Instructions for Use**

Oral administration for horses. Clenbuterol has not been used in small animals. It is prohibited for use in animals intended for food.

## Patient Monitoring and Laboratory Tests

Monitor heart rate in animals during treatment. Clenbuterol can be detected in urine for 12 days. Effective plasma concentrations are 500 pg/mL.

## Formulations

- Clenbuterol is available in 100- and 33-mL bottles of 72.5-mcg/mL syrup.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- No dose has been reported for small animals.

## Large Animal Dosage

### Horses

- Recurrent airway obstruction: 0.8 mcg/kg (0.008 mg/kg) twice daily PO. If initial dose is not effective, increase dose to two, three, and four times the initial dose, up to 3.2 mcg/kg. Duration of effect is approximately 6-8 hours.

## Regulatory Information

There are no withdrawal times established because clenbuterol should not be administered to animals that produce food. In horses, clenbuterol can be detected in urine for 12 days. Although not an approved human drug, it is abused in humans for weight loss and muscle building.

RCI Classification: 3

## Clindamycin Hydrochloride

klin-dah-mye'sin hye-droe-klor'ide

**Trade and other names:** Antirobe, ClinDrops, ClindaTobe, Clintabs, Clinsol, and generic (veterinary preparations) and Cleocin (human preparations)

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Antibacterial drug of the lincosamide class (similar in action to macrolides). It shares structural, microbiologic activity, and other properties with lincomycin. It inhibits bacterial protein synthesis via inhibition of bacterial ribosome. Clindamycin is bacteriostatic with a spectrum of activity primarily against gram-positive bacteria and anaerobes. Clindamycin, like the macrolide antibiotics, can concentrate in leukocytes and many tissues. Action of clindamycin is primarily against gram-positive organisms such as *Staphylococcus*, *Streptococcus*, and gram-positive rods such as *Corynebacterium*. Clindamycin also is active against mycoplasma and anaerobic organisms, although not all *Bacteroides* species are susceptible. Activity against *Toxoplasma* is controversial. The efficacy in animals is undetermined and in people it is a second-choice that requires high doses. In dogs the volume of distribution (VD) is 2.5 L/kg, the oral absorption is 73%, and the half-life is 4-4.5 hours after a dose of 5.5 mg/kg and 7-10 hours after a dose of 11 mg/kg.

## Indications and Clinical Uses

Clindamycin is primarily used for gram-positive or anaerobic bacterial infections involving the skin, respiratory tract, or oral cavity. Resistance with *Staphylococcus* may occur. It is effective for some oral infections and anaerobic infections. It also has been used for *Mycoplasma* infections. Efficacy of clindamycin for treating toxoplasmosis is controversial. Some studies have shown that clindamycin improved clinical signs, but it did not resolve the infection. Another study showed that clindamycin inhibited killing of *Toxoplasma* organisms by leukocytes.

## Precautionary Information

### Adverse Reactions and Side Effects

Oral clindamycin hydrochloride has been associated with esophageal lesions in cats. Oral liquid product may be unpalatable to cats, possibly because of the high alcohol content (8.6%). High doses have caused vomiting and diarrhea in cats. Clindamycin may alter the bacterial population in the intestine and cause diarrhea. Enteritis and diarrhea can be particularly serious in horses and ruminants.

### Contraindications and Precautions

Do not administer to rodents or rabbits because it may cause diarrhea. Do not administer orally to horses or ruminants because diarrhea, enteritis, and perhaps death can result. The oral liquid (Antirobe) contains 8.6% ethyl alcohol, which may be unpalatable to cats.

### Drug Interactions

Clindamycin injection should not be mixed with other drugs in the same vial, syringe, or IV line.

## Instructions for Use

Most doses are based on manufacturer's drug approval data and efficacy trials. Although every-12-hour frequency is recommended most often for dogs, there are studies that demonstrate efficacy when administered at 11 mg/kg every 24 hours for treatment of pyoderma. An injectable formulation is also available (Cleocin), which is clindamycin phosphate. This may be injected either IV or IM. If administering clindamycin IV, it should be diluted and administered by slow infusion (30-60 minutes). Dilution is usually 10:1 in 0.9% saline. It contains benzyl alcohol, and this vehicle has produced toxic reactions in young infants (and perhaps small animals).

## Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for susceptible organisms is  $\leq 0.25$  mcg/mL for streptococci and  $\leq 0.5$  mcg/mL for other organisms.

## Formulations

- Clindamycin is available in oral liquid (Aquadrops) 25 mg/mL; 25-, 75-, 150-, and 300-mg capsules; 25-, 75-, and 150-mg tablets; and 150-mg/mL injection (Cleocin).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Protect from freezing. Reconstituted solutions are stable for 2 weeks. Stability of compounded formulations is at least 60 days.

## Small Animal Dosage

### Dogs

- Staphylococcal infections: 11 mg/kg q12h PO or 22 mg/kg q24h PO. (Label dose for dogs is 5.5-33 mg/kg q12h PO.)
- Refractory infections: Doses up to 33 mg/kg q12h PO.
- Anaerobic infections and periodontal infections: 11-33 mg/kg q12h PO.
- 10 mg/kg q12h IV or IM. (For IV use, it should be diluted and administered by slow infusion.)

### Cats

- 5.5 mg/kg q12h or 11 mg/kg q24h PO. (Label dose for cats is 11-33 mg/kg q24h, PO.)
- Refractory infections: Doses up to 33 mg/kg q24h PO.
- Anaerobic infections and periodontal infections: 11-33 mg/kg q24h PO.
- Toxoplasmosis: 12.5 mg/kg, up to 25 mg/kg q12h for 4 weeks PO (see “[Indications and Clinical Uses](#)” section).
- 10 mg/kg q12h IV or IM. (For IV use, it should be diluted and administered by slow infusion.)

## Large Animal Dosage

- Do not administer clindamycin orally to large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Clodronate

Cloe-dronate

**Trade and Other Names:** OSPHOS

**Functional Classification:** Antihypercalcemic

## Pharmacology and Mechanism of Action

Bisphosphonate drug. Drugs in this class also include pamidronate, etidronate, tiludronate, ziludronate, and pyrophosphate. The clinical use of this class of drugs resides in their ability to inhibit bone resorption. These drugs decrease bone turnover by inhibiting osteoclast activity, inducing osteoclast apoptosis, retarding bone resorption, and decreasing the rate of osteoporosis. Inhibition of bone resorption is via inhibition of the mevalonate pathway. Bisphosphonates are classified as nitrogen-containing and non-nitrogenous based on the structure, with the nitrogen-containing drugs being more potent. Clodronate disodium is a non-nitrogen, chloro-containing bisphosphonate. After IM injection to horses at the label dose the half-life was  $1.65 \pm 0.52$  hours ( $T_{1/2}$ ) with a peak in 20 minutes.

## Indications and Clinical Uses

Clodronate is approved in the United States for treatment of bone pain associated with navicular syndrome in horses. Other bisphosphonate drugs are used in people to treat osteoporosis and treatment of hypercalcemia of malignancy. Other drugs in this class are helpful for managing complications associated with pathologic bone resorption. They also may provide pain relief in patients with pathologic bone disease.

Another bisphosphonate is tiludronate (Tildren), also approved for treating navicular disease in horses.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Reaction to clodronate has only been reported for horses. From field trials, the most commonly reported adverse effects were colic, agitation, and mild neurologic signs, such as tongue rolling and head shaking. Signs of colic usually occur shortly after drug administration (2 hours); therefore, monitor horses for at least 2 hours after injection. In most cases, these signs resolved within 5.5 hours following administration. Clinical pathology abnormalities associated with administration of OSPHOS included elevations in serum BUN, creatinine, glucose, and potassium concentrations and decreases in serum chloride concentrations. In safety studies, the most common adverse effects were clinical signs related to abdominal discomfort (colic), which was dose-related (more common at doses that exceeded label dose).

#### **Contraindications and Precautions**

Do not use in horses with kidney disease. Use carefully in conditions associated with hypocalcemia. It is not recommended to administer bisphosphonates to young growing animals. Do not use in pregnant mares as the safety in pregnancy has not been evaluated and bisphosphonates have caused fetal abnormalities of the bone when administered to laboratory animals.

#### **Drug Interactions**

Do not mix with solutions containing calcium (e.g., lactated Ringer's solution).

### **Instructions for Use**

Make sure horses are well hydrated prior to use to avoid kidney injury. Observe horses for 2 hours after administration for signs of colic.

### **Patient Monitoring and Laboratory Tests**

Monitor serum calcium and phosphorus. Monitor urea nitrogen, creatinine, urine-specific gravity, and signs of colic in treated animals.

### **Formulations**

Clodronate is available as 60 mg clodronate disodium per mL in 20 mL vial containing.

### **Stability and Storage**

Store at controlled room temperature 25°C (77°F) with deviations between 15°C-30°C (59°F-86°F) permitted.

### **Small Animal Dosage**

- No doses have been established for dogs or cats.

### **Large Animal Dosage**

#### **Horses**

- 1.8 mg/kg, IM. Maximum dose is 900 mg per horse. Divide the total volume equally into three separate injection sites.

### **Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Clofazimine

kloe-fah'zih-meen

**Trade and other names:** Lamprene

**Functional classification:** Antibacterial

C

### Pharmacology and Mechanism of Action

Antimicrobial agent used to treat feline leprosy. It produces a slow bactericidal effect on *Mycobacterium leprae*.

### Indications and Clinical Uses

Clofazimine has had limited use in veterinary medicine. Its use is limited to treating infections caused by *Mycobacterium*, such as feline leprosy.

#### Precautionary Information

##### Adverse Reactions and Side Effects

Adverse effects have not been reported in cats. In people, the most serious adverse effects are GI related.

##### Contraindications and Precautions

No contraindications reported for animals.

##### Drug Interactions

No drug interactions are reported in animals.

### Instructions for Use

Doses based on empiricism or extrapolation of human studies.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Clofazimine is available in 50-mg capsules.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Cats

- 1 mg/kg up to a maximum of 4 mg/kg/day PO.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).



## Clomipramine Hydrochloride

kloe-mip'rah-meen hye-droe-klor'ide

**Trade and other names:** Clomicalm (veterinary preparation) and Anafranil (human preparation)

**Functional classification:** Behavior modification

### Pharmacology and Mechanism of Action

Tricyclic antidepressant (TCA) drug. Used in people to treat anxiety and depression. Action is via inhibition of uptake of serotonin at presynaptic nerve terminals. Beneficial effects may be caused primarily by blocking reuptake of serotonin and modulation of serotonin in areas of the brain that affect anxiety and behavior. Clomipramine has more serotonin-reuptake-blocking effects than other TCA drugs. Side effects result from antimuscarinic effects caused by the active metabolite desmethylclomipramine. However, animals produce less of this metabolite than people do. In dogs, the half-life is 5 hours after oral administration, with a peak at 1.2 hours, but the half-life may be shorter (2-4 hours) with repeated dosing. The oral absorption in dogs is 20%.

### Indications and Clinical Uses

Like other TCAs, clomipramine is used in animals to treat various behavioral disorders, including obsessive-compulsive disorders (also called canine compulsive disorder) and separation anxiety. In dogs, it has been superior to amitriptyline for treating compulsive disorders; however, it does not appear to be beneficial when used for dominance-related aggression. In cats, with long-term treatment it has been effective for decreasing urine spraying (*J Am Vet Med Assoc*, 226: 378-382, 2005). It was equally effective as fluoxetine for urine spraying in cats, but treated animals returned to urine marking abruptly after the drug was discontinued. It has not been effective for psychogenic alopecia in cats.

### Precautionary Information

#### Adverse Reactions and Side Effects

Reported adverse effects include sedation and reduced appetite. Clomipramine has a bitter taste. Other side effects associated with TCAs are antimuscarinic effects (dry mouth, rapid heart rate, and urine retention) and antihistamine effects (sedation). In cats, sedation and weight gain have been observed. For clomipramine, antimuscarinic effects may be caused by an active metabolite. Clomipramine can decrease total  $T_4$  and free- $T_4$  thyroid concentrations in dogs, but it may still be within normal reference ranges. Overdoses can produce life-threatening cardiotoxicity. If an overdose occurs, immediately contact a poison control center. In trials performed in cats, no significant adverse effects were observed.

#### Contraindications and Precautions

Use cautiously in patients with heart disease.

#### Drug Interactions

Do not use with other behavior-modifying drugs such as serotonin reuptake inhibitors. Do not use with monoamine oxidase inhibitors (MAOIs), such as selegiline or amitraz.

## Instructions for Use

When adjusting doses, one may initiate therapy with a low dose and increase gradually. There may be a 2- to 4-week delay after initiation of therapy before beneficial effects are observed. After achieving a favorable response, the dose can be gradually lowered in some animals. In cats, doses of 1.25 to 2.5 mg per cat have been administered once daily for psychogenic alopecia. In cats, up to 5 mg once a day has been used for urine spraying.

## Patient Monitoring and Laboratory Tests

Monitor animal's heart rate and rhythm periodically during treatment. Like other TCAs, clomipramine may decrease total  $T_4$  and free- $T_4$  concentrations in dogs.

## Formulations

- Clomipramine is available in 20-, 40-, and 80-mg tablets (veterinary preparation) and 25-, 50-, and 75-mg capsules (human preparation).

## Stability and Storage

Store at room temperature. Protect from moisture. It has been compounded in a tuna-flavored liquid for cats without a decrease in efficacy.

## Small Animal Dosage

### Dogs

- 1-3 mg/kg/day q12h PO. Start at lower dose and gradually increase. Increases in dose should be made approximately every 14 days until desired effect is observed.

### Cats

- 1-5 mg per cat q12-24h PO (0.5 mg/kg per day) and gradually increase.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

## Clonazepam

kloe-nah'zih-pam

**Trade and other names:** Klonopin and generic brands

**Functional classification:** Anticonvulsant

## Pharmacology and Mechanism of Action

Benzodiazepine. Action is to enhance inhibitory effects of gamma-aminobutyric acid (GABA) in the central nervous system. Via GABA effects, it has anticonvulsant action, sedative properties, and effects on some behavioral disorders.

## Indications and Clinical Uses

Clonazepam has been used as an anticonvulsant in dogs and cats. As a benzodiazepine, it also is used to treat behavior problems in dogs and cats, particularly those associated with anxiety. Tolerance may develop to the anticonvulsant effects with long-term use.

**Precautionary Information****Adverse Reactions and Side Effects**

Side effects include sedation and polyphagia. Some animals may experience paradoxical excitement.

**Contraindications and Precautions**

No contraindications reported for animals.

**Drug Interactions**

No drug interactions are reported in animals. However, it will potentiate effects from other sedatives and CNS depressants.

**Instructions for Use**

Doses are based primarily on reports from human medicine, empiricism, or experimental studies. No clinical efficacy studies have been performed in dogs or cats.

Doses as low as 0.1-0.2 mg/kg have been used in animals susceptible to the higher doses listed in the dosage section.

**Patient Monitoring and Laboratory Tests**

Samples of plasma or serum may be analyzed for concentrations of benzodiazepines. However, many veterinary laboratories may not have this capability, and laboratories that analyze human samples may be nonspecific for benzodiazepines.

**Formulations**

- Clonazepam is available in 0.5-, 1-, and 2-mg tablets. Oral disintegrating tablets are available as 0.125-, 0.25-, 0.5-, 1-, and 2-mg.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Clonazepam, like other benzodiazepines, will exhibit adsorption to plastic, especially soft plastic (polyvinyl chloride). Compounded oral products are stable for 60 days.

**Small Animal Dosage****Dogs**

- 0.5 mg/kg q8-12h PO.

**Cats**

- 0.1-0.2 mg/kg q12-24h PO.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

Do not administer to animals intended for food.

Schedule IV controlled drug.

RCI Classification: 2

**Clopidogrel**

kloe-pid'oh-grel

**Trade and other names:** Plavix

**Functional classification:** Antiplatelet drug

## Pharmacology and Mechanism of Action

Clopidogrel is a platelet inhibitor. It is a thienopyridine and inhibits adenosine diphosphate (ADP) receptor-mediated platelet activity. A related drug is ticlopidine. Because this mechanism is different from the aspirin-inhibiting effect on platelets, clopidogrel is more effective than aspirin alone and has been used concurrently with aspirin. In dog, cats, and horses, oral administration has produced significant inhibitory effects on platelets that are superior to aspirin. Clopidogrel is metabolized to an active metabolite that exerts its antiplatelet effect. In cats, clopidogrel produced antiplatelet effects that persisted for 3 days after discontinuation of the drug. Clopidogrel administration also decreased serotonin release from platelets in cats, which may be important because serotonin release may contribute to clinical signs of thromboemboli in cats.

## Indications and Clinical Uses

Clopidogrel is used to inhibit platelets in patients that are prone to forming blood clots. In patients with a high risk for thrombi and emboli, clopidogrel will inhibit mechanisms that are not effected by aspirin alone. In cats, clopidogrel has been recommended to prevent cardiogenic arterial thromboembolism associated with heart disease. In dogs, it has been used to prevent embolism caused by heartworm disease and other conditions. In dogs, at a dose of either 0.5 or 1.0 mg/kg, decreased ADP-induced platelet aggregation occurs for 3 days after discontinuation of drug administration in some dogs and longer than 7 days in others. At 2 mg/kg orally, q24h, clopidogrel significantly suppressed platelet activity in horses, which persisted for 6 days after the last dose. A similar drug is ticlopidine (Ticlid), which should not be used in cats because it produces adverse reactions.

### Precautionary Information

Avoid use in animals that have bleeding problems; use cautiously with other drugs that may inhibit platelets or blood clotting.

### Adverse Reactions and Side Effects

Bleeding in susceptible patients. No adverse effects have been identified in cats, but in people, pruritus and skin rash have been reported.

### Contraindications and Precautions

Do not use in patients that have a high risk of bleeding. Discontinue several days prior to a planned surgical procedure.

### Drug Interactions

Use cautiously with other drugs that may inhibit blood clotting. In people, omeprazole (oral antiulcer agent) inhibits the conversion of clopidogrel to the active metabolite. It is not known if this interaction occurs in dogs, cats, or horses with clinical use.

## Instructions for Use

Administer with or without aspirin in patients prone to thrombi and emboli. The dose in cats of 19 mg is approximately one fourth of a human tablet. It is likely that smaller doses are effective, but they have not been evaluated because it is impractical to divide the human 75-mg tablet into fractions smaller than one fourth. The dose in dogs is usually 1 mg/kg q24h, PO. At this dose, the onset is 2 days, and steady-state is achieved in 5-7 days.

## Patient Monitoring and Laboratory Tests

Monitor for bleeding.

**Formulations**

- Clopidogrel is available in 75-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Cats**

- 18.75 mg per cat (one fourth of tablet) q24h PO.
- Smaller doses may be effective but have not been evaluated in cats.

**Dogs**

- 2 mg/kg q24h PO.
- An oral loading dose may be given at 2-4 mg/kg followed by 1-2 mg/kg q24h PO. (In some cases, a higher oral loading dose of 10 mg/kg has been used.)

**Large Animal Dosage****Horses**

- Loading dose of 4 mg/kg, followed by 2 mg/kg q24h PO.

**Regulatory Information**

Do not administer to animals that produce food.

**Cloprostenol Sodium**

Kloe pros' te nole

**Trade and other names:** Estrumate, estroPLAN

**Functional classification:** Prostaglandin

**Pharmacology and Mechanism of Action**

Cloprostenol is a synthetic prostaglandin, structurally related to PGF<sub>2</sub>-alpha, that produces PGF<sub>2</sub>-alpha effects. Synthetic prostaglandins are much more potent than natural prostaglandins, and one should not use these at the same dose as natural prostaglandins. Prostaglandin F<sub>2</sub> analogues have a direct luteolytic action on the corpus luteum. After injection, cloprostenol causes functional regression of the corpus luteum (luteolysis). In nonpregnant cycling cattle, this effect will result in starting estrus 2 to 5 days after injection. In pregnant animals, it will terminate pregnancy by inducing luteolysis and decreasing progesterone, followed by increasing myometrial contraction and increased uterine evacuation. In animals with prolonged luteal activity that have pyometra, mummified fetus, or luteal cysts, the luteolysis usually results in resolution of the problem and return to normal cycling.

**Indications and Clinical Uses**

Cloprostenol has been used in cattle to induce luteolysis (beef and dairy cattle) to manipulate the timing of the estrus cycle to benefit breeding management practices. It also can be used to terminate pregnancy resulting from undesired mating and to treat conditions associated with prolonged luteal function (e.g., pyometra, luteal cysts). Cloprostenol has been used to terminate pregnancy in any animal that forms a corpus luteum. Most reports on successful termination of pregnancy have been performed on cattle, horses, and dogs. In dogs, cloprostenol has been administered

in combination with other drugs (e.g., cabergoline [Dostinex] and bromocriptine [Parlodel]) to terminate pregnancy. When used to terminate pregnancy, it has been almost 100% effective. In cats, it was effective for treatment of pyometria in cats with an open cervix. In horses, it has been administered to induce premature labor in the last 2-4 weeks of pregnancy.

### Precautionary Information

#### Adverse Reactions and Side Effects

Induces abortion in pregnant animals. High doses in cattle (50 and 100 $\times$  dose) have caused discomfort, milk letdown, and some frothing. There are no long-term effects on fertility. Endometritis can occur in some animals after treatment for pyometra. When used to treat pyometra in dogs, panting, vomiting, nausea, and diarrhea can be seen 15-45 minutes after injection. In dogs, for termination of pregnancy, side effects have been mild but may include vomiting, nausea, and panting, occurring shortly after the injection and lasting for approximately 15-20 minutes. To avoid vomiting, it is recommended to wait 8 hours after feeding. Abortion may be followed by 1 week (approximately) of mucoid vulvar discharge. Mammary enlargement and mild milk production may occur in some dogs. In cats adverse effects after injection include vomiting, vocalization for up to 30 minutes, increased vaginal discharge, and diarrhea.

#### Contraindications and Precautions

Synthetic prostaglandins are much more potent than natural prostaglandins, so observe doses carefully to avoid overdose of the synthetic forms. Handle with caution. Women of childbearing age, asthmatics, and persons with bronchial and other respiratory problems should exercise extreme caution when handling this product. Cloprostenol is readily absorbed through the skin and may cause abortion and/or bronchospasms. Accidental spillage on the skin should be washed off immediately with soap and water. Do not administer to pregnant animals where the calf is not to be aborted.

### Instructions for Use

Give injections to cattle IM. When cloprostenol is injected in cattle, return to estrus activity usually occurs in 3-5 days, at which time animals may be inseminated. In some cases, a second injection may be given 11 days after the first injection (double-injection plan), with estrus occurring at 2-5 days after the second injection. When used to terminate pregnancy in cattle, it can be used any time from day 7 to 5 months after breeding, and the fetus is expelled usually after 4-5 days. In dogs, it has been used to terminate pregnancy approximately 30-40 days after breeding. In dogs, when used to terminate pregnancy, it has been used in combination with other drugs (bromocriptine or cabergoline) to allow for a lower dose of 1 mcg/kg, which has fewer side effects. Administer cloprostenol at least 8 hours after feeding to avoid vomiting.

### Patient Monitoring and Laboratory Tests

Monitor for continued vulvar discharge after treatment. Measurement of serum progesterone may be used to monitor therapy, especially if termination of abortion is prolonged.

### Formulations

- Cloprostenol is available in an injectable aqueous solution containing 250 mcg cloprostenol/mL. Dilution in saline is recommended for accurate dosing to dogs.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated, but prior to injection in small animals, it may be diluted with saline solution.

## Small Animal Dosage

### Dogs

- Terminate pregnancy: 1 to 2.5 mcg/kg once daily SQ, for 4-5 days, starting on day 25 after mating. (Side effects are lower with 1 mcg/kg.)
- Starting 35-45 days after mating, administer 1 mcg/kg SQ (after 10-fold dilution in saline) on days 1 and 3 of treatment. It can be administered with cabergoline (Galastop) 5 mcg/kg oral q24h on days 1 through 7 of treatment.
- 1 mcg/kg q48h SQ, administered with bromocriptine (see Bromocriptine for additional information).

### Cats

- Terminate pregnancy: 5 mcg/kg, SQ, once daily for 3 days

## Large Animal Dosage

### Cattle

- 2 mL (500 mcg) IM, once, or repeated again 11 days after the first injection.

### Horses

- Terminate pregnancy: 2 mL (500 mcg) per horse, IM. In some conditions, repeated injections are administered (e.g., every 12 hours). To induce premature labor in the last 2-4 weeks of pregnancy, administer two doses 30 minutes apart (oxytocin also is used for this indication). For endometritis, 250 mcg (1 mL) IM twice, 12 hours apart, usually combined with oxytocin.

## Regulatory Information

To be used only by licensed veterinarians. No withdrawal times are listed on approved label for food animals.

## Clorazepate Dipotassium

klor-az'eh-pate dye-poe-tah'see-um

**Trade and other names:** Tranxene and generic

**Functional classification:** Anticonvulsant

## Pharmacology and Mechanism of Action

Benzodiazepine. Clorazepate is one of the active metabolites of diazepam, producing similar effects as diazepam but longer acting. After oral absorption, it is quickly converted to the active drug, referred to as nordiazepam or desmethyldiazepam. Similar to diazepam and other benzodiazepines, its action is to enhance inhibitory effects of GABA in the CNS.

## Indications and Clinical Uses

Clorazepate is used for antiseizure action, sedation, and treatment of some behavioral disorders. It has been used in dogs and cats when other drugs are not effective. It has been used in refractory epileptics, but tolerance may develop to the anticonvulsant effects with long-term use. It is not recommended as a sole treatment for seizure disorders in dogs and cats.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects include sedation and polyphagia. Some animals may experience paradoxical excitement. Chronic administration may lead to dependence and a withdrawal syndrome if discontinued.

### Contraindications and Precautions

No serious contraindications. In rare individuals, benzodiazepines have caused paradoxical excitement. They may cause fetal abnormalities early in pregnancy, but this has not been reported with veterinary use.

### Drug Interactions

No drug interactions are reported in animals. However, it will potentiate effects from other sedatives and CNS depressants.

## Instructions for Use

Doses are based primarily on reports from human medicine, empiricism, or experimental studies. Higher doses may be used for short-term treatment of noise phobia. However, for most indications, no clinical efficacy studies have been performed in dogs or cats. Clorazepate tablets degrade quickly in the presence of light, heat, or moisture.

## Patient Monitoring and Laboratory Tests

Samples of plasma or serum may be analyzed for concentrations of benzodiazepines. If response to clorazepate is measured, the active metabolite, nordiazepam (desmethyldiazepam), should be measured. Plasma concentrations in the range of 100-250 ng/mL have been cited as the therapeutic range for people. Other references have cited this range as 150 to 300 ng/mL. However, there are no readily available tests for monitoring in many veterinary laboratories. Laboratories that analyze human samples may have nonspecific tests for benzodiazepines. With these assays, there may be cross-reactivity among benzodiazepine metabolites.

## Formulations Available

- Clorazepate is available in 3.75-, 7.5-, and 15-mg tablets.

## Stability and Storage

Keep in original packaging or store in tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 0.5-2 mg/kg q8-12h PO, and as frequently as 4 hours. (Total dose is usually 3.75 mg or 7.5 mg.)

### Cats

- 0.2-0.4 mg/kg q12-24h, up to 0.5-2.2 mg/kg q12h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 2



## Cloxacillin Sodium

kloks-ah-sill'in soe'dee-um

**Trade and other names:** Cloxapen, Orbenin, and Tegopen

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Inhibits bacterial cell wall synthesis by binding to penicillin-binding proteins. Cloxacillin is similar in spectrum and activity as amoxicillin, except that it is resistant to the beta-lactamase enzyme produced by *Staphylococcus*. The spectrum is limited to gram-positive bacteria, especially staphylococci. Methicillin-resistant *Staphylococcus* species are resistant to cloxacillin.

### Indications and Clinical Uses

The spectrum of cloxacillin includes gram-positive bacilli, including beta-lactamase-producing strains of *Staphylococcus*. Therefore it has been used to treat staphylococcal infections in animals, including pyoderma. Because of the availability of other beta-lactam drugs for treating gram-positive infections such as those caused by *Staphylococcus*, cloxacillin is used infrequently in small animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects of penicillin drugs are most commonly caused by drug allergy. This can range from acute anaphylaxis when administered to other signs of allergic reaction when other routes are used. When administered orally (especially with high doses), diarrhea is possible.

#### Contraindications and Precautions

Use cautiously in animals allergic to penicillinlike drugs.

#### Drug Interactions

No drug interactions are reported in animals. However, do not mix with other drugs because inactivation may result.

### Instructions for Use

Doses based on empiricism or extrapolation from human studies. No clinical efficacy studies available for dogs or cats. Oral absorption is poor; if possible, administer on an empty stomach.

### Patient Monitoring and Laboratory Tests

Culture and sensitivity testing: Use oxacillin as a guide for sensitivity testing.

### Formulations

- Cloxacillin is available in 250- and 500-mg capsules and 25-mg/mL oral solution.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 20-40 mg/kg q8h PO.

## Large Animal Dosage

- No dose has been reported for large animals. The only formulation approved for food animals is Dariclox, a 20 mg/mL intramammary infusion. Dose is 10 mL (200 mg) per infected quarter q12h for 3 treatments.

## Regulatory Information

Dairy cows (intramammary use) withdrawal time for milk: 30 days for dry-cow treatment. Cattle withdrawal time for meat: 10 days for meat and 48 hours for milk for the lactating cow treatment.

## Codeine

Koe'deen

**Trade and other names:** Generic, codeine phosphate, and codeine sulfate

**Functional classification:** Analgesic, opioid, antitussive

## Pharmacology and Mechanism of Action

Opiate agonist, analgesic. Mechanism is similar to morphine, except with approximately one tenth the potency of morphine. Codeine is extensively metabolized. In dogs, oral absorption is low (<5%), but it is rapidly converted to other metabolites that may have analgesic activity, such as glucuronidated forms of codeine. The activity of codeine and perhaps some active metabolites is to bind to mu receptors and kappa-opiate receptors on nerves and inhibit release of neurotransmitters involved with transmission of pain stimuli (such as substance P). It also may inhibit release of some inflammatory mediators. Central sedative and euphoric effects are related to mu-receptor effects in brain.

## Indications and Clinical Uses

Codeine, or codeine with acetaminophen, is indicated for treatment of moderate pain. It also has been used as an antitussive. Despite the widespread use of codeine in humans, the efficacy in animals for its antitussive or analgesic use has not been established. Oral absorption in dogs is low. Because a small portion of codeine is converted to morphine (only 10% in people) and duration of morphine is short in dogs, the clinical effectiveness of codeine in dogs may be questionable.

## Precautionary Information

### Adverse Reactions and Side Effects

Like all opiates, side effects from codeine are predictable and unavoidable. Side effects include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses.

### Contraindications and Precautions

Schedule II controlled substance. Tolerance and dependence occur with chronic administration. High doses (60-mg tablet with acetaminophen) can cause sedation in dogs. Cats are more susceptible to excitement than other species. Some codeine formulations may contain other ingredients (e.g., acetaminophen) that should not be administered to cats.

### Drug Interactions

No drug interactions are reported in animals. However, it will potentiate effects from other sedatives and CNS depressants.

## Instructions for Use

Available as codeine phosphate and codeine sulfate oral tablets. Doses listed for analgesia are considered initial doses; individual patients may need higher doses depending on degree of tolerance or pain threshold. When administering acetaminophen–codeine combinations, the high-dose tablet (containing 60 mg codeine) tends to cause sedation in dogs (body weight 20–30 kg), and the lower dose (containing 30 mg) is recommended.

## Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, if necessary, atropine can be administered. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

## Formulations

- Codeine is available in 15-, 30-, and 60-mg tablets; 5-mg/mL syrup; and 3-mg/mL oral solution. It is also available in formulations with acetaminophen. Note that many of the syrups have other ingredients that may not be appropriate for pets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- Analgesia: 0.5–1 mg/kg q4–6h PO.
- Antitussive: 0.1–0.3 mg/kg q4–6h PO.

### Cats

- Analgesia: 0.5 mg/kg q6h PO. Increase dose as needed to control pain.
- Antitussive: 0.1 mg/kg q6h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Drug controlled by Drug Enforcement Administration (DEA). Schedule II; some antitussive forms are Schedule V.

RCI Classification: 1

## Colchicine

Kol' chih-seen

**Trade and other names:** Colcrys and generic brands

**Functional classification:** Anti-inflammatory agent

## Pharmacology and Mechanism of Action

Anti-inflammatory agent. It inhibits fibrosis and formation of collagen.

## Indications and Clinical Uses

In people, colchicine is used to treat gout. In animals, it has been used as an antifibrotic agent to decrease fibrosis and development of hepatic failure (possibly by inhibiting formation of collagen). However, the efficacy for controlling liver fibrosis in chronic liver disease is questionable and unproven. Anti-inflammatory effects may be caused by inhibition of neutrophil and mononuclear migration. Antifibrotic effects result from blockage of microtubular-mediated transcellular movement of

proteins and to inhibit secretion of procollagen molecules into the extracellular matrix. It has also been used in animals to control amyloidosis. In Shar Pei dogs, colchicine has been used to treat a fever syndrome, possibly because of its use in people for treating Mediterranean fever.

### Precautionary Information

#### Adverse Reactions and Side Effects

The most common adverse effects are nausea, vomiting, abdominal pain, and diarrhea. Because there is a risk of vomiting, diarrhea, and decreased appetite in dogs, and there is little evidence of antifibrotic effect for chronic liver disease in dogs, the use in dogs with liver disease is discouraged. Colchicine may cause dermatitis in people, but this has not been reported in dogs or cats.

#### Contraindications and Precautions

Do not administer to pregnant animals.

#### Drug Interactions

There are no drug interactions reported for small animals.

### Instructions for Use

Doses are based on empiricism. There are no well-controlled efficacy studies in veterinary species.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Colchicine is available in 600-mcg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 0.01-0.03 mg/kg q24h PO.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Colony-Stimulating Factors: Sargramostim and Filgrastim

**Trade and other names:** Leukine and Neupogen

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Stimulates granulocyte development in bone marrow. Two drugs in this class include filgrastim (rG-CSG) and sargramostim (rGM-CSF).

**Indications and Clinical Uses**

Colony-stimulating factors are used primarily to regenerate blood cells to recover from cancer chemotherapy or other bone marrow-suppressing therapy. Their use is uncommon in animals.

**Precautionary Information****Adverse Reactions and Side Effects**

Pain at injection site. Edema has been reported in people.

**Contraindications and Precautions**

There are none identified in small animals.

**Drug Interactions**

There are no drug interactions reported for small animals.

**Instructions for Use**

Doses are based on limited experimental information and extrapolations from human experience. To prepare sargramostim, add 1 mL to make up 250-mcg/mL or 500-mcg/mL vial. Dilute further with 0.9% saline solution to less than 10 mcg/mL for infusion. Do not shake vial to prevent foaming; gently swirl vial to mix contents.

**Patient Monitoring and Laboratory Tests**

Monitor CBC to assess treatment. Treatment can be discontinued when neutrophils recover.

**Formulations**

- Colony-stimulating factors are available in 300 mcg/mL (Neupogen) and 250 and 500 mcg/mL (Leukine).

**Stability and Storage**

Store in a tightly sealed container protected from light.

**Small Animal Dosage****Dogs and Cats**

- Sargramostim: 250 mcg/m<sup>2</sup> (0.25 mg/m<sup>2</sup>) IV infusion over 2 hours, or SQ.
- Filgrastim: 5 mcg/kg (0.005 mg/kg) once daily, SQ, for 2 weeks, or 10 mcg/kg/day.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

Do not administer to animals intended for food.

**Corticotropin**

kor-tih-koe-troe'pin

**Trade and other names:** Acthar

**Functional classification:** Hormone

## Pharmacology and Mechanism of Action

Corticotropin (ACTH). Corticotropin is a natural peptide hormone, composed of 39 amino acids. The formulation is prepared into a gel for injection. It stimulates normal synthesis of cortisol and other hormones from adrenal cortex.

## Indications and Clinical Uses

Adrenocorticotrophic hormone is used for diagnostic purposes to evaluate adrenal gland function. Another closely related synthetic product, cosyntropin, is used for the same purpose. The availability of Acthar gel has been limited, and cosyntropin is often used as a substitute (see [cosyntropin](#) section for more details). Compounded formulations may not be equivalent.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects unlikely when used as a single injection for diagnostic purposes.

#### Contraindications and Precautions

Do not administer IV.

#### Drug Interactions

There are no drug interactions reported for small animals.

## Instructions for Use

Doses are established by measuring normal adrenal response in animals. See also Cosyntropin, which is sometimes preferred for clinical use. However, availability and cost of cosyntropin and ACTH are the factors that usually determine which is used in small animals.

## Patient Monitoring and Laboratory Tests

Monitor cortisol concentrations. Post-ACTH cortisol response should be as follows:

Dogs 5.5-20.0 mcg/dL; > 20 mcg/dL is consistent with hyperadrenocorticism.

Cats 4.5-15 mcg/dL; > 15 mcg/dL is consistent with hyperadrenocorticism.

Following treatment for hyperadrenocorticism (e.g., treatment with mitotane), response should be 1-5 mcg/dL.

## Formulations

- Adrenocorticotrophic hormone is available in 80-units (international units)/mL gel.

## Stability and Storage

Store in a tightly sealed container protected from light.

## Small Animal Dosage

### Dogs

- ACTH response test: Collect pre-ACTH sample and inject 2.2 samples and inject 2.2 units (IU)/kg IM. Collect post-ACTH sample at 2 hours.

### Cats

- ACTH response test: Collect pre-ACTH sample and inject 2.2 units (IU)/kg IM. Collect post-ACTH sample at 1.5 and 2 hours.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No withdrawal times are available. Because clearance is rapid and there is little risk from residues, no withdrawal time is suggested for food animals.

## Cosyntropin

koe-sin-troe'pin

**Trade and other names:** Cortrosyn, synthetic corticotropin, tetracosactrin, and tetracosactide

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Cosyntropin (beta-corticotropin) is a synthetic form of the peptide hormone corticotropin (ACTH) that is identical to the N-terminal 24 residues of natural corticotropin. It is also known in international formularies as tetracosactrin or tetracosactide. Cosyntropin is an aqueous solution, whereas ACTH is a gel. Therefore cosyntropin can be administered IV, but ACTH gel cannot. Cosyntropin is also more potent than ACTH. Administration of cosyntropin will stimulate secretion of cortisol from adrenal glands. Administration of cosyntropin also will stimulate secretion of sex hormones of adrenal origin.

### Indications and Clinical Uses

Cosyntropin is used for diagnostic purposes to evaluate adrenal gland function in dogs, cats, and horses. Maximum peak cortisol secretion occurs at 60-90 minutes (30 minutes in horses). It is used for the same purpose as corticotropin, but in humans it is preferred over corticotropin because it is less allergenic.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are unlikely when used as a single injection for diagnostic purposes. In people, cosyntropin is preferred over ACTH gel because cosyntropin is less allergenic.

#### Contraindications and Precautions

Maximum dose for dogs should be 250 mcg.

#### Drug Interactions

There are no drug interactions reported for small animals.

### Instructions for Use

Use for diagnostic purposes only; it is not intended for treatment of hypoadrenocorticism. Cosyntropin is preferred to ACTH gel because it is available in a formulation that is easier to use in dogs and cats. In dogs, cosyntropin has been administered at 5 mcg/kg IV or IM and 250 mcg/dog IM. All three protocols produce similar results, and IM injection produces similar results as IV injection. In cats, similar response is observed with 125 mcg per cat and 5 mcg/kg. In horses, 0.1 mcg/kg IV produced maximum response in 30-90 minutes. Compounded formulations of ACTH may produce similar results at 60 minutes postinjection, but may have lower cortisol concentrations at 90 and 120 minutes compared with a proprietary formulation. One may split reconstituted Cortrosyn into aliquots of 50 mcg each (250-mcg vial split into 5 aliquots) or 25 mcg each (250-mcg vial split into 10 aliquots) and frozen in plastic syringes.

## Patient Monitoring and Laboratory Tests

Monitor cortisol concentrations. Post-ACTH cortisol response should be as follows:

Dogs: 5.5-20.0 mcg/dL; >20 mcg/dL is consistent with hyperadrenocorticism. More specifically, 5.5-17 mcg/dL normal, 17-25 mcg/dL borderline, 25-30 mcg/dL suggestive, and >30 mcg/dL highly likely for hyperadrenocorticism.

If monitoring sex hormones of adrenal origin, a sample for analysis should be taken at 60 minutes after injection.

Cats: 4.5-15 mcg/dL; >15 mcg/dL is consistent with hyperadrenocorticism.

Following treatment for hyperadrenocorticism (e.g., treatment with mitotane), response should be 1-5 mcg/dL.

## Formulations

- Cosyntropin is available in 250 mcg per vial. The lyophilized powder is reconstituted in 2 mL vials.

## Stability and Storage

Once prepared, this formulation can be kept in the refrigerator for 4 months. Frozen cosyntropin can be stored in aliquots. For example, it can be stored in small plastic syringes and frozen at  $-20^{\circ}\text{C}$  for up to 6 months, or in the refrigerator for 4 months. Some compounded formulations are stable and have produced reliable results at the 60-minute sample but may be lower at the 120-minute sample compared to the proprietary preparation.

## Small Animal Dosage

### Dogs

- Response test: Collect precosyntropin sample and inject 5 mcg/kg IV or IM and collect postsample at 30 and 60 minutes or one sample at 60 minutes. Maximum dose for dogs should be 250 mcg. The following guidelines can be used for dosing: less than 5 kg, 25 mcg; 5-10 kg, 50 mcg; 10-15 kg, 75 mcg; 15-20 kg, 100 mcg; 20-25 kg, 125 mcg; 25-30 kg, 150 mcg; 30-40 kg, 200 mcg; 40-50 kg, 225 mcg; and more than 50 kg, 250 mcg (1 vial).

### Cats

- Response test: Collect precosyntropin sample and inject 125 mcg (0.125) per cat IV or IM per cat and collect postsample at 60 and 90 minutes after IV administration or at 30 and 60 minutes after IM administration. Alternatively, similar results can be expected when injecting 5 mcg/kg followed by sample collection at 60 and 75 minutes.

## Large Animal Dosage

### Horses

- 0.1 mcg/kg IV produces maximum adrenal stimulation, with peak cortisol concentration in 30-90 minutes. Not recommended as a reliable test in horses.

### Foals

- (ACTH Stimulation test): 0.25 mcg/kg IV. Peak cortisol occurs at 20-30 minutes.

## Regulatory Information

No withdrawal times are available. Because clearance is rapid and there is little risk from residues, no withdrawal time is suggested for animals intended for food.



## Cyanocobalamin

syehahn-oh-koe-bahl'ah-min

**Trade and other names:** Cobalamin, Vitamin B<sub>12</sub>

**Functional classification:** Vitamin

### Pharmacology and Mechanism of Action

Vitamin B<sub>12</sub> supplement.

### Indications and Clinical Uses

Vitamin B<sub>12</sub> has been used to treat some conditions of anemia. Vitamin B<sub>12</sub> is used to manage vitamin B deficiencies associated with cobalt deficiency, inadequate intake, or intestinal malabsorption. In patients with exocrine pancreatic insufficiency (EPI) or IBD, particularly cats, deficiency of cobalamin is common and supplementation is recommended. Vitamin B<sub>12</sub> is a water-soluble vitamin and absorption in the intestine is a receptor-mediated process. It is dependent on the intrinsic factor produced by the pancreas and animals with intestinal disease may have difficulty with absorption. Cats are particularly susceptible because they cannot store cobalamin as well as people and they lack the binding protein transcobalamin-1. Thus, cats have a much more rapid turnover than people. The half-life in people is 1 year; but in healthy cats it is 11-14 days, or 4.5-5.5 days in cats with intestinal disease.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are rare, except in high overdoses, because water-soluble vitamins are easily excreted in the urine.

#### Contraindications and Precautions

No contraindications reported for animals.

#### Drug Interactions

There are no drug interactions reported for small animals.

### Instructions for Use

Not necessary to supplement in animals with well-balanced diets. But in cats, especially cats with intestinal disease, supplementation is recommended in deficient cats (explanation provided above). In these cats, weekly supplementation is recommended.

### Patient Monitoring and Laboratory Tests

Cobalamin concentrations can be measured in most laboratories. Recommended plasma/serum concentrations are as follows: dogs, 252-908 ng/L and cats, 290-1500 ng/L. Less than 160 ng/mL in cats is clearly deficient. Monitor CBC when used to treat anemia.

### Formulations

- Cyanocobalamin is available in tablets ranging from 25 to 1000 mcg. Injection formulations range from 1000 to 5000 mcg/mL (1 to 5 mg/mL). Vitamin B complex solutions may contain 10-100 mcg/mL of vitamin B<sub>12</sub>.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 100-200 mcg/day PO or 250-500 mcg/day IM or SQ.

### Cats

- 50-100 mcg/day PO or 250 mcg IM or SQ, weekly. If levels are maintained with once-weekly injections for 6 weeks, increasing the interval to 2 weeks, 4 weeks, and 6 weeks (incrementally) can be attempted.

## Large Animal Dosage

### Calves and Foals

- 500 mcg once per foal or calf, twice weekly IM or SQ.

### Lambs and Pigs

- 500 mcg once per lamb or pig, twice weekly IM or SQ.

### Cattle and Horses

- 1000-2000 mcg per horse or cattle, once or twice weekly IM or SQ.

## Regulatory Information

No withdrawal times are available. Because clearance is rapid and there is little risk from residues, no withdrawal time is suggested for animals intended for food.

## Cyclophosphamide

syeh-kloee-foss'fah-mide

**Trade and other names:** Cytoxan, Neosar, and CTX

**Functional classification:** Anticancer agent

## Pharmacology and Mechanism of Action

Cytotoxic and anticancer agent. Cyclophosphamide belongs to the group of nitrogen mustards. They are alkylating agents (bifunctional alkylating agents) that alkylate various macromolecules but preferentially alkylate the N-7 of the guanine base of DNA. They are cytotoxic to cancer cells and are toxic to the rapidly dividing cells of the bone marrow. Cyclophosphamide must be metabolized to active metabolites for pharmacologic effect, which requires P450 enzyme activation. The metabolites hydroxyphosphamide and aldophosphamide are cytotoxic. Aldophosphamide is converted at the tissue site to phosphoramidate mustard and acrolein. Phosphoramidate mustard is responsible for the antitumor effect, and acrolein is responsible for the cytotoxic action that causes toxicity (e.g., hemorrhagic cystitis). The half-life of the parent drug in dogs is 4-6.5 hours.

## Indications and Clinical Uses

Cyclophosphamide is used primarily as an adjunct for cancer chemotherapy and as immunosuppressive therapy. Cyclophosphamide is probably the most potent of the nitrogen mustards. It is used in chemotherapy protocols for a variety of tumors, carcinomas, sarcomas, feline lymphoproliferative diseases, mast cell tumor, mammary carcinoma, and especially lymphoproliferative tumors (lymphoma). Cancer protocols such as cyclophosphamide, Oncovin, and prednisone (COP) and cyclophosphamide, hydroxydaunomycin, Oncovin, and prednisone (CHOP) incorporate cyclophosphamide as one of the agents. Cyclophosphamide is also used as continuous treatment

for some cancers—also known as metronomic dosing. The advantage of metronomic dosing is decreased adverse effects (lower dose), and other benefits such as decreased angiogenesis in tumors (decreased proliferation), decreased vascular endothelial growth factor (VEGF), and decreases circulating T-regulatory cells (T-reg). See dosing section for metronomic protocol. The other major use of cyclophosphamide is for immunosuppression. Although it has been used for various immune-mediated disorders in animals (immune-mediated hemolytic anemia (IMHA), pemphigus, systemic lupus erythematosus [SLE]), efficacy has not been reported in controlled studies for these diseases. In one trial it was shown that cyclophosphamide (50 mg/m<sup>2</sup>) had no benefit over prednisolone alone for treatment of IMHA (*J Vet Intern Med*, 17: 206-212, 2003).

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Cyclophosphamide is toxic to the bone marrow in a dose-dependent manner. After a single large bolus dose, the nadir of toxicity occurs in 7-10 days, but the effect is reversible because stem cells are usually unaffected. Recovery usually occurs in 21-28 days. Vomiting and diarrhea may occur in some patients. Sterile, hemorrhagic cystitis is a serious and limiting complication to therapy in dogs. It is caused by the toxic effects of metabolites on the bladder epithelium (especially acrolein) that are concentrated and excreted in the urine. Various attempts are used to decrease the injury to the bladder epithelium. Corticosteroids are usually administered with cyclophosphamide to induce polyuria and decrease inflammation of the bladder. The drug mesna (Mesnex, mercaptoethane sulfonate) provides free active thiol groups to bind metabolites of cyclophosphamide in the urine. Furosemide (2.2 mg/kg) administered at the same time as the cyclophosphamide dose may decrease risk of sterile hemorrhagic cystitis. Cats are less susceptible to developing cystitis compared to dogs. Cyclophosphamide may cause hair loss when used in some chemotherapeutic protocols. Dogs most susceptible are those with continuously growing hair (e.g., poodles and Old English sheepdogs). Cats do not tend to lose hair from cyclophosphamide treatment.

#### **Contraindications and Precautions**

Bone marrow suppressive and immunosuppressive. Use cautiously in animals at risk for infection. Teratogenic and embryotoxic. Do not use in pregnancy.

#### **Drug Interactions**

Use cautiously with other drugs that may cause bone marrow suppression. Although this drug is highly metabolized to active metabolites, it is not known what effect other drugs have on enzyme activity.

### **Instructions for Use**

Cyclophosphamide is usually administered with other drugs (other cancer drugs in cancer protocols or corticosteroids when used for immunosuppressive therapy). Consult specific anticancer protocols for specific regimens. For example, the COAP protocol (COAP is a combination of cyclophosphamide, vincristine, prednisolone, and cytosine arabinoside) uses 50 mg/m<sup>2</sup> orally, every 48 hours, with vincristine, cytosine arabinoside, and prednisone for 8 weeks, but one CHOP protocol uses 100-150 mg/m<sup>2</sup> IV on the first day of the protocol, followed by other drugs such as doxorubicin, vincristine, and prednisone. In dogs, the maximum tolerated dose is 500 mg/m<sup>2</sup> IV (with autologous bone marrow support).

## Patient Monitoring and Laboratory Tests

Monitor CBC in animals during treatment. Monitor urinalysis in dogs during treatment.

## Formulations

- Cyclophosphamide is available in 25-mg/mL injection and 25- and 50-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Tablets are coated and should not be split in order to retain stability. Do not let temperatures exceed 30° C. Subject to hydrolysis in aqueous solutions. Use reconstituted solutions within 24 hours at room temperature and within 6 days if refrigerated, although some refrigerated solutions have been stable for 60 days.

## Small Animal Dosage

### Dogs

- Anticancer dose: 50 mg/m<sup>2</sup> (approx. 2.2 mg/kg) q48h or once daily 4 days/week PO. Alternatively, some protocols use 150-300 mg/m<sup>2</sup> IV and repeat in 21 days.
- Metronomic dose (continuous administration to suppress T cells): 10-15 mg/m<sup>2</sup>, q24h, PO (approximately 0.3 mg/kg).
- Immunosuppressive therapy: Dogs: 50 mg/m<sup>2</sup> q48h PO or 2.2 mg/kg once daily for 4 days/week.
- Pulse therapy: 200-250 mg/m<sup>2</sup> (10 mg/kg), once every 3 weeks. Dividing the 250 mg/m<sup>2</sup> dose into three treatments, over three days, may reduce risk of sterile hemorrhagic cystitis.

### Cats

- 6.25-12.5 mg/cat once daily 4 days/week.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Cyclosporine, Cyclosporin A

Sye'kloe-spor-een

**Trade and other names:** Atopica (veterinary preparation), Neoral (human preparation), Sandimmune, Optimmune (ophthalmic), Gengraf, and generic brands. In the US it is called cyclosporine; the international name is ciclosporin.

**Functional classification:** Immunosuppressive drug

## Pharmacology and Mechanism of Action

Immunosuppressive drug. Cyclosporine binds to a specific cellular receptor on calcineurin and inhibits the T-cell receptor-activated signal transduction pathway. Particularly important are its effects to suppress interleukin-2 (IL-2) and other cytokines and block proliferation of activated T-lymphocytes. The action of cyclosporine is more specific for T-cells as compared to B-cells. However, the production of antibodies by B cells requires the help of activated T cells. Calcineurin inhibitors such as cyclosporine may decrease humoral immune response by interfering with T-helper cells

instead of interfering directly. Cyclosporine also inhibits the mitochondrial permeability-transition pores that may attenuate myocardial injury during reperfusion. The half-life of cyclosporine is 8-9 hours (average) in dogs and 8-10 hours (average) in cats. However, there is high variability on both species. Oral absorption is low (20%-30%) and may be affected by food and drug interactions. Peak concentration after oral administration occurs at 1-2 hours. The average peak concentration (with high variability) in dogs is approximately 900 ng/mL (600-1200 ng/mL) at 5 mg/kg.

### **Indications and Clinical Uses**

Systemic uses (usually oral) for cyclosporine include IMHA, atopic dermatitis in dogs, and perianal fistulas. Other diseases have been treated with cyclosporine, such as sebaceous adenitis, idiopathic sterile nodular panniculitis, immune-mediated hemolytic anemia (IMHA), immune-mediated thrombocytopenia (ITP), inflammatory bowel disease (IBD), immune-mediated polyarthritis, myasthenia gravis, and aplastic anemia. It has also been used for treatment of granulomatous meningoencephalitis (3-6 mg/kg q12h). In dogs, evidence is well-established for treatment of atopic dermatitis, for which there is similar efficacy as prednisolone. Treatment response may be delayed for two weeks, and for as long as four weeks in some dogs. During this induction time, it is acceptable to administer other medications (e.g., corticosteroids or oclacitinib) to control pruritus in dogs with atopic dermatitis. However, there is minimal effectiveness for immune-mediated pemphigus foliaceus (PF) in dogs, but may have benefits for treating pemphigus foliaceus in cats. In dogs, some dermatologists have reported improved efficacy when combined with azathioprine for immune-mediated diseases (e.g., pemphigus foliaceus). Cyclosporine use for keratoconjunctivitis sicca (KCS) is limited to topical administration. In cats, cyclosporine has shown beneficial effects for treatment of eosinophilic granuloma complex, IBD, atopic dermatitis (60% effective), oral stomatitis, and airway disease (feline asthma). Cyclosporine (Atopica for cats) is approved for control of feline allergic dermatitis. Higher doses are needed in cats compared to dogs because the oral absorption is more variable. In horses, it is effective as a localized treatment of anterior uveitis.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

The most common adverse effects in dogs and cats are gastrointestinal problems (vomiting, diarrhea, anorexia, and weight loss). Cyclosporine may induce new hair growth in dogs. Neurotoxicity from high doses has been seen in dogs, which can be seen as tremors. However, this is uncommon from recommended doses. Although kidney injury has been reported with older formulations, it has not been reported from use of current formulations of cyclosporine. Less commonly, cyclosporine can produce gingival proliferation (gingival hyperplasia) in animals. Occasionally gingivitis and periodontitis may occur, which can be reversed after discontinuing the drug. Cyclosporine can inhibit pancreatic beta cells. It may increase tissue insulin resistance and impair insulin production or secretion to increase glycemia. However, diabetes has not been reported in pets from clinical use of cyclosporine. Papillomas have been observed in dogs with chronic use. Unlike other immunosuppressive drugs, it does not cause myelosuppression.

*Effect on vaccination:* At three times the clinical dose, it did not affect the immune response to killed rabies vaccine in dogs, but it failed to increase antibody titers from live parvovirus vaccine. Cats treated with cyclosporine, even at high doses, are capable of mounting a memory humoral immune response to booster vaccination (FCV, PV, FeLV, FHV-1, and rabies) that is adequate for protection. However, at high doses a primary humoral response was not observed within 4 weeks of

exposure to a novel antigen (FIV). Therefore, naïve cats vaccinated before cyclosporine treatment should be able to mount an adequate primary immune response, and subsequent cyclosporine treatment should not affect immune response from booster vaccinations.

*Effect on infections in cats:* Administration to cats at 7.5 mg/kg did not increase the severity of infection by *Toxoplasma gondii* in cats that were previously exposed (seropositive). However, administration of cyclosporine to cats that are naïve (seronegative) may increase the severity of *T. gondii* infection. Naïve cats may have a greater risk of developing clinical toxoplasmosis if they become infected while receiving cyclosporine treatment. Do not administer to cats infected with feline leukemia virus (FeLV) or feline immunodeficiency virus (FIV). In cats infected with feline herpes virus (FHV-1), administration of cyclosporine activated the infection but the disease was mild and self-limited in most cats.

### Contraindications and Precautions

At high doses, cyclosporine has produced embryotoxic and fetotoxic effects in laboratory animals. It is not recommended to administer to pregnant animals. It is excreted in milk of lactating animals. Warn animal owners to keep out of reach of children. If used with other drugs, consult “Drug Interactions” section for possible interference.

### Drug Interactions

Cimetidine, erythromycin, itraconazole, fluconazole, clarithromycin, or ketoconazole may increase cyclosporine concentrations when used concurrently. Doses of ketoconazole of 2.5 to 10 mg/kg/day in dogs have been shown to substantially decrease the clearance of cyclosporine and reduce the required dose by one half or more. Grapefruit juice also inhibits clearance and will reduce the required dose, although high doses are needed. For example, 10 grams of powdered whole grapefruit is needed in dogs to substantially affect exposure (such a large dose of 42 capsules is impractical). Food will decrease oral absorption by 15%-22%. Metoclopramide and rifampin (and possibly other drugs that induce enzymes) will lower cyclosporine blood concentrations. There is no evidence that cyclosporine enhances, or inhibits allergen-specific immunotherapy (ASIT) treatment.

### Instructions for Use

Atopica (veterinary) and Neoral (human) are identical formulations, except that sizes of capsules vary. After animals have been treated with initial doses of 5 mg/kg per day and are stable, doses may be adjusted by increasing the interval to once every other day or every third day, rather than lowering daily dose. Individual doses may be adjusted by monitoring blood concentrations, but monitoring is not necessary for routine use. Atopica and Neoral oral products are absorbed more predictably than Sandimmune. Atopica and Neoral may produce 50% higher blood concentrations in some patients or reduce the variability in absorption that was associated with the Sandimmune formulations. There are over 20 human generic formulations but none have been tested for bioequivalence in dogs or cats. Feeding may reduce oral absorption in dogs but does not decrease efficacy. For cats, it is recommended to administer with food. Generic formulations are available for humans, but have not been evaluated for bioequivalence to Atopica in dogs. Oral solution can be diluted to make it more palatable. To reduce the dose, some veterinarians have administered ketoconazole or other enzyme-inhibiting compounds concurrently. When used to treat animals for organ transplantation, the doses are generally higher and the blood concentrations maintained at a higher level.

## Patient Monitoring and Laboratory Tests

Although routine blood concentration monitoring is not necessary, it may be helpful to identify drug interactions, poor absorption, adverse reactions, or poor compliance. However, there has been no correlations established between blood concentrations in dogs and cats and clinical response. When monitoring, collect whole blood in ethylenediaminetetraacetic acid (EDTA; purple top) tube for submission to laboratory. Suggested trough blood concentration range (whole blood assay) is 300-400 ng/mL, although in some studies, levels as low as 200 ng/mL have been effective. Peak concentrations (collected at approximately 2 hours after oral administration of 5 mg/kg) should be in the range of 600-1200 ng/mL. Consult the laboratory to determine if the laboratory result is specific, or if it also measures inactive metabolites and requires a conversion. Cyclosporine does not interfere with intradermal skin testing.

## Formulations

- Cyclosporine is available in 10-, 25-, 50-, and 100-mg capsules (Atopica) and 25 and 100 microemulsion capsules. Atopic for cats is available as 100 mg/mL oral solution. Human forms are also available as 100-mg/mL oral solution (Neoral, for microemulsion); 100-mg/mL oral solution and 25- and 100-mg capsules (Sandimmune); and 0.2% ophthalmic ointment (Optimmune). Generic human capsules are available, (e.g., Gengraf). The human generic formulations are therapeutically equivalent in people but have not been compared in dogs or cats to Atopica.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not refrigerate, but store at below 30° C. Compounded ophthalmic products are stable at room temperature for 60 days, but do not refrigerate.

## Small Animal Dosage

### Dogs

- 3-7 mg/kg/day PO. The typical starting dose is 5 mg/kg/day PO. After induction period, some dogs with atopic dermatitis have been controlled with doses as low as 5 mg/kg every other day to every third day.
- For perianal fistulas and immune-mediated diseases (e.g., IMHA), higher doses and more frequent administration have been used (5-8 mg/kg, every 12 hours). When a response is observed the dose and frequency can be reduced.
- For immune suppression associated with organ transplantation, doses should be higher (e.g., 7-10 mg/kg q12h PO).
- Inflammatory bowel disease: 5 mg/kg PO q12h, then reduce the frequency to q24h after a response is observed.

### Cats

- 7.5 mg/kg per day, PO. Some cats can be controlled with administration of this dose every other day, or twice weekly. Administer on a small amount of food, or at the time of feeding.
- For immune suppression associated with organ transplantation, doses should be higher (e.g., 3-5 mg/kg q12h PO).

## Large Animal Dosage

- Only local administration has been used in horses (ocular). No other dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it may have mutagenic potential.

## Cyproheptadine Hydrochloride

Sih'proe-hep'tah-deen hye-droe-klor'idē

**Trade and other names:** Periactin

**Functional classification:** Antihistamine

C

### Pharmacology and Mechanism of Action

Phenothiazine with antihistamine and antiserotonin properties. Used as appetite stimulant (probably by altering serotonin activity in appetite center).

### Indications and Clinical Uses

A common use of cyproheptadine is to stimulate the appetite in sick animals, especially cats; although, evidence based on controlled studies to demonstrate efficacy is not available. Cyproheptadine is used in some cats for treatment of feline asthma if serotonin is considered a component of the airway inflammation. However, in cats with hyperresponsive airways, cyproheptadine failed to reduce eosinophilic inflammation (8 mg per cat q12h). It has been used in some instances for treating inappropriate urination (urine spraying) in cats. Cyproheptadine has been used to treat equine pituitary pars intermedia dysfunction (Cushing syndrome) at 0.6-1.2 mg/kg, but results have been controversial. It is not effective for treatment of canine pituitary-dependent hyperadrenocorticism (Cushing syndrome). It has been considered as a treatment for animals that have “serotonin syndrome” from antidepressant drugs, although efficacy has not been documented for this use.

### Precautionary Information

#### Adverse Reactions and Side Effects

Stimulates hunger. May cause polyphagia and weight gain. Cyproheptadine also has antihistamine effects, antiserotonin effects, and antimuscarinic effects. In some cats, it has stimulated hyperactivity. In horses, it has been used at high doses without adverse effects.

#### Contraindications and Precautions

None reported for animals.

#### Drug Interactions

There are no drug interactions reported for small animals.

### Instructions for Use

Clinical studies have not been performed in veterinary medicine. Use is based primarily on empiricism and extrapolation from human results. Syrup contains 5% alcohol.

### Patient Monitoring and Laboratory Tests

Monitor weight gain in animals.

### Formulations Available

- Cyproheptadine is available in 4-mg tablets and 2-mg/5 mL syrup.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze the syrup. Stability of compounded formulations has not been evaluated.



**Small Animal Dosage****Dogs and Cats**

- Antihistamine: 0.5-1.1 mg/kg q8-12h PO, or 2-4 mg/cat PO q12-24h.
- Appetite stimulant: 2 mg/cat PO.
- Feline asthma: 1-2 mg/cat PO q12h.
- Use for inappropriate urination: 2 mg/cat q12h PO, then reduce dose to 1 mg/cat q12h PO.

**Large Animal Dosage****Horses**

- 0.5 mg/kg q12h PO.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

**Cytarabine**

syə-tarə'ah-been

**Trade and other names:** Cytosar, Ara-C, and cytosine arabinoside

**Functional classification:** Anticancer agent

**Pharmacology and Mechanism of Action**

Anticancer agent. Cytarabine (Cytosar) is a compound isolated from a sea sponge. It has also been referred to as *cytosine arabinoside* and *Ara-C*. Cytarabine is metabolized to an active drug that inhibits DNA synthesis. Cytarabine is an anti-metabolite synthetic nucleoside analogue. Cytarabine A inhibits DNA polymerase in mitotically active cells and produces topoisomerase dysfunction and prevents DNA repair. The half-life in dogs is approximately 70 minutes. When administered to dogs, the terminal half life of cytarabine was 1.35 hours and 1.15 hours after SQ and constant rate infusions, respectively. Peak concentrations were 2.9 mcg/ml and 2.8 mcg/mL after SQ and CRI administration respectively.

**Indications and Clinical Uses**

Cytarabine has been used for lymphoma and leukemia protocols. It is used in small animals for treatment of lymphoma and myelogenous leukemia. It is usually administered as an IM or SQ injection because it has a short half-life (approximately 20 minutes) when administered IV. It has also been administered to dogs for treatment of granulomatous meningoencephalomyelitis as an alternative to corticosteroids. Cytarabine penetrates the blood-CSF barrier of dogs and has been reported to improve the temporary and long term remission and prognosis for dogs diagnosed with meningoencephalitis. Two protocols are used for this indication (see [dosing](#) section). When administered via constant rate infusion (CRI) to dogs, it maintains steady-state concentrations better than a SQ injection.

**Precautionary Information****Adverse Reactions and Side Effects**

Cytarabine is bone marrow suppressive and can cause granulocytopenia, especially when delivered via CRIs. In addition, it may cause nausea and vomiting.

### Contraindications and Precautions

Use cautiously in animals administered other bone marrow-suppressing drugs.

### Drug Interactions

There are no drug interactions reported for small animals.

### Instructions for Use

Cytarabine has been administered to dogs using a variety of protocols (see [dosing](#) section), depending on the study published and dependent on clinician preference. There is not strong evidence that one protocol is superior to another. When treating granulomatous meningoencephalomyelitis, dose protocols (either IV or SQ) have used total doses of 200-400 mg/m<sup>2</sup> total dose, divided over 2 days, either as SQ injections twice daily for 2 days or an IV infusion with the total dose given over 8 hours.

The dose of cytarabine commonly used in the treatment of meningoencephalitis is a total dose of 200 mg/m<sup>2</sup>, lower than that used in the treatment of neoplasia (total dose of 400 to 600mg/m<sup>2</sup>). For meningoencephalitis, veterinary neurologists have recommended 200 mg/m<sup>2</sup> administered either as four subcutaneous (SQ) injections of 50 mg/m<sup>2</sup> given over two days or continuous rate intravenous (CRI) administration at 25 mg/m<sup>2</sup> per hour for 8 hours.

### Patient Monitoring and Laboratory Tests

Monitor CBC to assess toxicity.

### Formulations

- Cytarabine is available in a 100-mg vial for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### *Dogs (Cancer Protocols, Administered Weekly)*

- 100-150 mg/m<sup>2</sup> once daily or 50 mg/m<sup>2</sup> twice daily, each given for 4 days IV or SQ.
- 600 mg/m<sup>2</sup>, IV or SQ, single dose.
- 300 mg/m<sup>2</sup> per day as a continuous IV infusion, over 48 hours (600 mg/m<sup>2</sup> total).

#### *Dogs (Granulomatous Meningoencephalomyelitis)*

- 50 mg/m<sup>2</sup> twice daily for 2 days and repeated every 3 weeks SQ.
- 200 mg/m<sup>2</sup> total dose, administered as 50 mg/m<sup>2</sup> given four times over two days subcutaneously or continuous rate intravenous (CRI) administration at 25 mg/m<sup>2</sup> per hour for 8 hours.

### Cats

- 100 mg/m<sup>2</sup> once daily for 2 days.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Dacarbazine

dah-kar'bah-zeen

**Trade and other names:** DTIC

**Functional classification:** Anticancer agent

### Pharmacology and Mechanism of Action

Anticancer agent. Dacarbazine (DTIC) is a monofunctional alkylating agent; thus it effectively blocks RNA synthesis. Its action is cell-cycle nonspecific.

### Indications and Clinical Uses

DTIC has been primarily used for malignant melanoma and lymphoreticular neoplasms.

### Precautionary Information

#### Adverse Reactions and Side Effects

The most common adverse effects are leukopenia, nausea, vomiting, and diarrhea.

#### Contraindications and Precautions

Do not use in cats.

#### Drug Interactions

There are no drug interactions reported for small animals.

### Instructions for Use

Consult anticancer protocol for specific regimens.

### Patient Monitoring and Laboratory Tests

Monitor complete blood count (CBC) during treatment.

### Formulations

- DTIC is available in a 200-mg vial for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 200 mg/m<sup>2</sup> for 5 days q3wks IV or 800-1000 mg/m<sup>2</sup> q3wks IV.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Dalteparin

dahl'tah-pare-in

**Trade and other names:** Fragmin and LMWH

**Functional classification:** Anticoagulant

**D**

### Pharmacology and Mechanism of Action

Low-molecular-weight heparin (LMWH), also known as fragmented heparin. Low-molecular-weight heparin is characterized by a molecular weight of approximately 5000, compared to conventional heparin (unfractionated heparin, or UFH) with a molecular weight of approximately 15,000. Subsequently, the absorption, clearance, and activity of LMWH differ from UFH. Low-molecular-weight heparins produce their effect by binding to antithrombin (AT) and increasing AT III-mediated inhibition of synthesis and activity of coagulation factor Xa. However, LMWH, unlike conventional heparin, produces less inhibition of thrombin (factor IIa). Low-molecular-weight heparin's activity is described by the anti-factor Xa/anti-factor IIa ratio. For dalteparin, the ratio is 2.7:1 (the conventional UFH ratio is 1:1). In people, LMWHs have several advantages compared to UFH and include greater anti-Xa/IIa activity, more complete and predictable absorption from injection, longer duration, less frequent administration, reduced risk of bleeding, and a more predictable anticoagulant response. However, in dogs and cats, the half-life of LMWH is much shorter than in humans, reducing some of this advantage. In dogs, the half-life of dalteparin is approximately 2 hours; in cats, it is estimated to be 1.5 hours, which requires much more frequent administration in either species to maintain anti-Xa activity compared to humans. Low-molecular-weight heparins used in veterinary medicine include tinzaparin (Innohep), enoxaparin (Lovenox), and dalteparin (Fragmin).

### Indications and Clinical Uses

Dalteparin, like other LMWHs, is used to treat hypercoagulability disorders and prevent coagulation disorders such as thromboembolism, venous thrombosis, disseminated intravascular coagulopathy (DIC), and pulmonary thromboembolism. Clinical indications are derived from uses of conventional heparin or extrapolated from human medicine. There have been few clinical studies to examine efficacy of LMWH in animals. Previously published doses extrapolated from humans (100 units/kg q12h, SQ) have been shown not to produce adequate and consistent anti-Xa activity in dogs and cats, and the doses listed in this entry are needed for therapy. In people, enoxaparin has largely replaced dalteparin for routine use.

### Precautionary Information

#### Adverse Reactions and Side Effects

Although better tolerated than regular heparin, bleeding is a risk. Low-molecular-weight heparins are associated with a lower incidence of heparin-induced thrombocytopenia in people, but heparin-induced thrombocytopenia from any form of heparin has not been a clinical problem in animals. If excessive anticoagulation and bleeding occur as a result of an overdose, protamine sulfate should be administered to reverse heparin therapy. The protamine dose is 1.0 mg protamine for every 100 U dalteparin administered by slow IV infusion. Protamine complexes with heparin to form a stable, inactive compound.

#### Contraindications and Precautions

Do not administer IM to prevent hematoma; administer SQ only. Low-molecular-weight heparin is excreted by renal clearance in animals; therefore if renal disease

is present, the elimination will be prolonged. Rebound hypercoagulability may occur after discontinuation of heparin treatment; therefore it may be advised to taper the dose slowly when discontinuing treatment.

### Drug Interactions

Do not mix with other injectable drugs. Use cautiously in animals that are already receiving other drugs that can interfere with coagulation, such as aspirin and warfarin. Although a specific interaction has not been identified, use cautiously in animals that may be receiving certain chondroprotective compounds such as glycosaminoglycans for treatment of arthritis. Some antibiotics, such as cephalosporins, may inhibit coagulation.

### Instructions for Use

Dosing recommendations extrapolated from human medicine are not appropriate for animals. Animal owners should be warned that LMWHs are expensive compared to conventional heparin. When dosing, do not interchange doses on a unit-for-unit basis with other heparins.

### Patient Monitoring and Laboratory Tests

Monitor patients for clinical signs of bleeding problems. When administering LMWH, activated partial thromboplastin time (aPTT) and prothrombin time (PT) clotting times are not reliable indicators of therapy, although prolonged aPTT is a sign of overdosing. In people, a-Xa activity is considered the preferred laboratory measure of LMWH activity. However, in studies in which anti-Xa activity was monitored in dogs, it resulted in inconsistent attainment of the targeted range. Peak anti-Xa activity occurs 2 hours after dosing, and the target range for anti-Xa activity should be 0.5-1.0 U/mL for cats and 0.4-0.8 U/mL for dogs.

### Formulations

- Dalteparin is available in 2500 units anti-factor Xa (16 mg dalteparin sodium) per 0.2 mL in a single-dose syringe, 5000 units anti-factor Xa (32 mg dalteparin sodium) per 0.2 mL in a single-dose syringe, and 10,000 units anti-factor Xa (64 mg dalteparin sodium) per mL in a 9.5 mL multiple-dose vial.

### Stability and Storage

Use multiple-dose vial within 2 weeks of initial penetration. Store in a tightly sealed container protected from light.

### Small Animal Dosage

#### Dogs

- 150 U/kg, q8h, SQ (see monitoring section for dose adjustment).

#### Cats

- 150-175 U/kg, q4h, SQ, to 180 U/kg q6h, SQ (see “[Patient Monitoring and Laboratory Tests](#)” section for dose adjustment).

### Large Animal Dosage

#### Horses

- 50 U/kg/day SQ. High-risk patients should receive 100 U/kg/day.

### Regulatory Information

Extralabel withdrawal times are not established. However, 24-hour withdrawal times are suggested because this drug has little risk from residues.

## Danazol

dan'ah-zole

**Trade and other names:** Danocrine

**Functional classification:** Hormone

**D**

### Pharmacology and Mechanism of Action

Gonadotropin inhibitor. Danazol suppresses luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and estrogen synthesis. Danazol has been used as adjunctive treatment for immune-mediated blood disorders. Its mechanism of action for treating immune-mediated diseases is not understood, but it may interfere with antibody production or the binding of complement or antibody to the platelet or red blood cell. It may also reduce receptors on monocytes for antibodies bound to platelets or red blood cells.

### Indications and Clinical Uses

Danazol has hormone effects (antiestrogen) that are used for endometriosis in women. Danazol (Danocrine) also has been used for treating refractory patients with immune-mediated thrombocytopenia and immune-mediated hemolytic anemia. However, available evidence does not show a benefit in dogs when it has been used to treat immune-mediated hemolytic anemia.

### Precautionary Information

#### Adverse Reactions and Side Effects

Danazol's androgenic effects should be considered in treated animals. However, adverse effects have not been reported in animals.

#### Contraindications and Precautions

It is absolutely contraindicated in pregnancy.

#### Drug Interactions

It has been used with other drugs in the treatment of immune-mediated diseases without reported interactions.

### Instructions for Use

When used to treat autoimmune disease, it is usually used in conjunction with other drugs (e.g., corticosteroids).

### Patient Monitoring and Laboratory Tests

Monitor CBC if used for treatment of immune-mediated diseases.

### Formulations

- Danazol is available in 50-, 100-, and 200-mg capsules.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 5-10 mg/kg q12h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Danazol is an anabolic agent and should not be administered to animals intended for food.

Racing Commissioners International (RCI) Classification: 4

## Danofloxacin Mesylate

dan-oh-floks'ah-sin mess'ih-late

**Trade and other names:** A180

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Danofloxacin, like other fluoroquinolones, has activity against a broad spectrum of bacteria, including gram-negative bacilli, especially *Enterobacteriaceae* (*Escherichia coli*, *Klebsiella*, *Salmonella*) and some gram-positive cocci, such as *Staphylococcus*. In particular, it has good activity against pathogens in cattle, such as *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni* (formerly *Haemophilus somnus*). In cattle, subcutaneous absorption is high. Half-life is 3-6 hours.

When used to treat bovine respiratory disease (BRD) in cattle at a dose of 6 mg/kg, danofloxacin had a half-life of 4.2 hours, a peak concentration of 1.7 mcg/mL, and produced area under the curve (AUC):minimum inhibitory concentration (MIC) ratio >125.

## Indications and Clinical Uses

Danofloxacin is indicated for the treatment of BRD caused by *P. multocida*, *M. haemolytica*, and *H. somni* (formerly *H. somnus*). As a fluoroquinolone with a broad spectrum of activity, other organisms are susceptible. However, extralabel use for other diseases in animals intended for food is prohibited. There are no published reports of danofloxacin use in other animals.

## Precautionary Information

### Adverse Reactions and Side Effects

All fluoroquinolones at high concentrations may cause central nervous system (CNS) toxicity. In safety studies in cattle, when high doses were administered, they caused lameness, articular cartilage lesions, and CNS problems (tremors, nystagmus, etc.). Subcutaneous injections may cause tissue irritation. All of the fluoroquinolones have a potential to produce arthropathy in young animals. In field trials, danofloxacin was associated with lameness in some calves. Fluoroquinolones have caused blindness in cats, but this has not been reported in any species from danofloxacin.

### Contraindications and Precautions

Do not inject more than 15 mL in one site. Do not use extralabel. Do not use in other species for which safety information is not available. Do not use in animals prone to seizures.

### Drug Interactions

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

## Instructions for Use

Inject SQ in neck of cattle.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. Clinical and Laboratory Standards Institute (CLSI) break points for sensitive organisms are  $\leq 0.25$  mcg/mL for cattle respiratory pathogens. Most organisms have MIC values  $\leq 0.06$  mcg/mL.

## Formulations

- Danofloxacin is available in an injectable solution of 180 mg/mL (with 2-pyrrolidone and polyvinyl alcohol).

## Stability and Storage

Store below 30° C, protected from light, and protected from freezing. A slight yellow or amber color is acceptable.

## Small Animal Dosage

### Dogs and Cats

- No small animal dose has been reported.

## Large Animal Dosage

### Cattle

- 6 mg/kg (1.5 mL per 100 pounds), once per 48 hours, SQ.

### Equine and Swine

- No dose has been reported.

## Regulatory Information

Do not use in calves intended for veal.

Cattle withdrawal time (for meat): 4 days. Not established for milk because it cannot be used in lactating cattle. It is prohibited to use extralabel.

## Dantrolene Sodium

dan'troe-leen soe'dee-um

**Trade and other names:** Dantrium, Revonto, Ryanodex

**Functional classification:** Muscle relaxant

## Pharmacology and Mechanism of Action

Muscle relaxant. Dantrolene inhibits calcium leakage from sarcoplasmic reticulum. It is specific for the *RyR1* isoform (sarcoplasmic reticulum channel) in skeletal muscle and *RyR3* in smooth muscle, with minimal effect on the *RyR2* in cardiac muscle. By inhibiting calcium initiation of muscle contraction, it relaxes muscle. In horses, after oral administration, the half-life was 3.4 hours with a peak at 30 minutes. In dogs the half-life is 1.25 hours and pharmacokinetics are markedly different than in people.

## Indications and Clinical Uses

Dantrolene is used as a muscle relaxant. However, in addition to muscle relaxation, it has been used to treat muscle excitability associated with malignant hyperthermia, and it also has been used to relax urethral muscle in cats. Although it has been used in dogs, the efficacy has not been shown and pharmacokinetic studies show that at a dose of 2.8 mg/kg it does not produce concentration high enough for activity in canine muscle. Although used as an immunosuppressive agent (via NFAT-regulated cytokine suppression), it is unlikely to be effective for this use.



In horses, it has improved clinical signs associated with exertional rhabdomyolysis (“tying up”). It can prevent muscle damage in healthy horses. It has been used as a pre-anesthetic in horses to prevent anesthetic myopathy, but exact dose for this problem is undetermined.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Muscle relaxants can cause weakness in some animals. Use of dantrolene in people has caused hepatitis in some cases. In horses, when administered prior to anesthesia at a dose of 6 mg/kg orally (premedication) it increased plasma potassium concentrations and increased risk of bradycardia and arrhythmias in some horses. Hyperkalemia from dantrolene also has been observed in dogs and pigs. In people, it is known to cause muscle weakness, dyspnea, dysphagia, and dizziness.

#### **Contraindications and Precautions**

Do not use in animals with hepatic disease. Use with caution in weak or debilitated animals.

#### **Drug Interactions**

Do not mix or reconstitute the IV solution with acidic solutions because they are incompatible.

### **Instructions for Use**

It is usually recommended that oral doses should be given on an empty stomach. Doses have been primarily extrapolated from experimental studies or extrapolation of human studies. Few studies are available in veterinary medicine. To relax the urethra in cats, the most effective dose is 1 mg/kg IV. When administering dantrolene for treatment of malignant hyperthermia in large animals, several vials may be needed because of dilute solution in vial.

### **Patient Monitoring and Laboratory Tests**

When used for treatment of malignant hyperthermia, monitor body temperature, acid-base balance, and electrolytes. In people, dantrolene may cause hepatitis, and tests of liver injury (e.g., liver enzymes) and/or function are monitored. Dantrolene can cause a persistent increase in plasma potassium concentration during anesthesia. The increase in potassium may lead to cardiac arrhythmias and should be monitored.

### **Formulations**

- Dantrolene is available in 100-mg capsules; when reconstituted, the 20-mg vial is equal to 0.33 mg/mL injection. Also available as a more concentrated single-dose vial containing 250 mg reconstituted to 50 mg/mL.

### **Stability and Storage**

When IV solution is prepared, it is stable for a short time (6 hours). It may be mixed with solutions such as 5% dextrose and 0.9% sodium chloride. Do not use IV solution if cloudiness or precipitation is present in vial. Compounded oral suspensions are stable for 150 days if mixed with acid solutions (e.g., citric acid). Store in a tightly sealed container, protected from light, and at room temperature.

### **Small Animal Dosage**

#### **Dogs**

**Note:** doses cited below for dogs are from anecdotal experience and extrapolation from humans. Pharmacokinetic studies suggest that these doses are unlikely to produce concentrations high enough to be effective in canine muscle.

- Prevention of malignant hyperthermia: 2-3 mg/kg IV, (up to 5-10 mg/kg).

- Malignant hyperthermia crisis: doses of 2.5-3 mg/kg IV rapid bolus (up to 5-10 mg/kg).
- Muscle relaxation: 1-5 mg/kg q8h PO (up to 5-10 mg/kg).
- Urethral relaxation: 1-5 mg/kg q8h PO or 0.5-1.0 mg/kg IV (up to 5-10 mg/kg).

#### Cats

- Muscle relaxation: 0.5-2 mg/kg q12h PO.
- Relaxation of urethra: 1-2 mg/kg q8h PO.

### Large Animal Dosage

#### Horses

- 4 mg/kg PO.

#### Pigs

- Malignant hyperthermia: 1-3 mg/kg IV once.
- Prophylaxis: 5 mg/kg PO.

### Regulatory Information

For horses, there is a recommended 48 hour and 168 hour withdrawal time prior to racing for detection in plasma and urine, respectively. For food animals, no regulatory information is available. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Dapsone

dap'sone

**Trade and other names:** Generic brands

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Antimicrobial drug used for treatment of mycobacterium. It may also have some immunosuppressive properties or inhibit function of inflammatory cells.

### Indications and Clinical Uses

Although originally used as an antibacterial drug, in veterinary medicine it is used primarily for dermatologic diseases in dogs, especially subcorneal pustular dermatosis and dermatitis herpetiformis. It also has been used for canine pemphigus.

### Precautionary Information

#### Adverse Reactions and Side Effects

Hepatitis and blood dyscrasias may occur. Because it shares similar properties as a sulfonamide, the same reactions seen with sulfonamides can be seen with dapsone and include anemia, neutropenia, thrombocytopenia, hepatotoxicosis, and skin-drug eruptions. It is toxic to cats and will cause neurotoxicosis and anemia.

#### Contraindications and Precautions

Do not administer to cats. Do not administer to animals that are sensitive to sulfonamides.

**Drug Interactions**

Use caution when administering dapsone with trimethoprim/sulfonamide combinations. Trimethoprim may increase blood concentrations of dapsone because it inhibits excretion and potentiates dapsone adverse effects.

**Instructions for Use**

Doses are derived from extrapolation of human doses or empiricism. No well-controlled clinical studies have been performed in veterinary medicine.

**Patient Monitoring and Laboratory Tests**

Monitor for signs of hepatic reactions. Monitor CBC occasionally because bone marrow toxicity has occurred in some animals.

**Formulations**

- Dapsone is available in 25- and 100-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Dapsone may discolor without change in potency. Compounded suspension formulations have been stable for 21 days when mixed with citric acid.

**Small Animal Dosage****Dogs**

- 1.1 mg/kg q8-12h PO.

**Cats**

- Do not use.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Darbepoietin Alfa**

DAR-be-POE-e-tin AL-fa

**Trade and Other Names:** Aranesp

**Functional Classification:** Hormone

**Pharmacology and Mechanism of Action**

Human recombinant erythropoietin. Hematopoietic growth factor that stimulates erythropoiesis. Darbepoetin is a hyperglycosylated recombinant form of human erythropoietin. It differs from epoetin because it has 5 N-carbohydrate chains, thus producing a longer duration. The longer half-life translates to less often administration. In dogs it has a 3 times longer half-life than epoetin. It has been used in people to treat anemia associated with chronic kidney disease.

**Indications and Clinical Uses**

Darbepoetin alfa is used to treat nonregenerative anemia. It has been used to treat myelosuppression caused by disease or chemotherapy. It also has been used to treat chronic anemia associated with chronic kidney disease, particularly in cats, with apparent success based on anecdotal accounts. The dose listed is based on anecdotal experiences in cats. The typical dose in people is 2.25 mcg/kg once every 3 weeks. A similar agent used in animals is erythropoietin (epoetin alpha). A conversion for treatment is: 400 units/week of epoetin = 1 mcg/kg darbepoetin.

## Precautionary Information

### Adverse Reactions and Side Effects

Because this product is a human-recombinant product, it may induce local and systemic allergic reactions in animals. Injection site pain and headache have occurred in people. Adverse effects have included iron deficiency, hypertension, joint pain (arthralgia), gastrointestinal disturbance, and polycythemia. Human erythropoietin products can cause red cell aplasia due to neutralizing anti-erythropoietin antibodies that cross-react with other forms of erythropoietin. The feline erythropoietin is 83% homologous to human erythropoietin. Increased red cell aplasia may occur in animals because of less than 100% homology and more antibody production.

### Contraindications and Precautions

Do not shake vial vigorously. Do not dilute with other fluids or solutions. Do not use if cloudy. Stop therapy if joint pain, fever, anorexia, or cutaneous reactions are observed. Rotate sites of injection to avoid reactions.

### Drug Interactions

No interactions are reported.

## Instructions for Use

The use of darbepoetin has been primarily in cats with anemia caused by chronic kidney disease. Iron supplementation is recommended when used in cats. By improving anemia in cats, it may increase survival for cats with chronic kidney disease and improve quality of life.

## Patient Monitoring and Laboratory Tests

Monitor hematocrit. Dose should be adjusted to maintain hematocrit in a range of 25%-35%.

## Formulations Available

Darbepoietin alfa is available in a variety of injectable solution concentrations, including: 25-, 40-, 60- 100-, 200-, 300- and 500- mcg/mL.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze. Do not mix with other solutions or fluids.

## Small Animal Dosage

### Dogs

- Dose not established for dogs. Similar doses as used in cats have been used.

### Cats

- Start with 1 mcg/kg once per week until the target PCV is achieved. Then, the frequency can be decreased to every 2-3 week intervals. Typically the expected response is a PCV of 25-35%.

## Large Animal Dosage

No large animal doses are reported.

## Regulatory Information

No withdrawal times are established for food animals. Erythropoietin or derivatives in any form is prohibited to be on the premises of racing horses.

RCI Classification: 2

**Deferoxamine Mesylate**

deh-fer-oks'ah-meen mess'ih-late

**Trade and other names:** Desferal**Functional classification:** Antidote**Pharmacology and Mechanism of Action**

Chelating agent with strong affinity for trivalent cations. Because of its ability to bind to and chelate cations, it is used to treat acute iron toxicosis.

**Indications and Clinical Uses**

Deferoxamine is indicated in cases of severe poisoning, especially iron toxicosis. It also has been used to chelate aluminum and facilitate removal.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects have not been reported in animals. Allergic reactions and hearing problems have occurred in people.

**Contraindications and Precautions**

Administer IV formulation slowly to avoid precipitation of cardiac arrhythmias. Deferoxamine is teratogenic. Do not use in pregnant animals unless the benefits outweigh the risks.

**Drug Interactions**

Deferoxamine will chelate with cations; avoid mixing with cations prior to administration.

**Instructions for Use**

100 mg of deferoxamine binds 8.5 mg of ferric iron. Contact local poison control center for guidance on dosing after an overdose.

**Patient Monitoring and Laboratory Tests**

Monitor serum iron concentrations to determine severity of intoxication and success of therapy. Successful therapy is indicated by monitoring urine color (orange-rose color change to urine indicates chelated iron is being eliminated).

**Formulations**

- Deferoxamine is available in a 500-mg and 2 gram vial for injection.

**Stability and Storage**

Deferoxamine is soluble in water. Stable when stored in solution for 14 days. Store in a tightly sealed container, protected from light, and at room temperature. Do not refrigerate and do not mix solutions with other medications.

**Small Animal Dosage****Dogs and Cats**

- 15 mg/kg/hour IV infusion, or 40 mg/kg IM q4-6 h, or 40 mg/kg slow IV injection q4-6h for chelation of iron. The treatment is generally continued 24 hours.

**Large Animal Dosage**

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. There are no anticipated problems from levels of residues in animals. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Deracoxib

dare-ah-koks'ib

**Trade and other names:** Deramaxx

**Functional classification:** Anti-inflammatory

## Pharmacology and Mechanism of Action

Deracoxib is a nonsteroidal anti-inflammatory drug (NSAID). Like other drugs in this class, deracoxib produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the cyclo-oxygenase (COX) enzyme. The COX enzyme exists in two isoforms called *COX-1* and *COX-2*. *COX-1* is primarily responsible for synthesis of prostaglandins important for maintaining a healthy gastrointestinal (GI) tract, renal function, platelet function, and other normal functions. *COX-2* is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of *COX-1* and *COX-2* effects in some situations, and *COX-2* activity is important for some biological effects. Deracoxib, using in vitro assays, is more *COX-1* sparing compared to older NSAIDs and is a selective inhibitor of *COX-2*. The *COX-1/COX-2* ratio is high compared to some other drugs registered for dogs. It also is a selective *COX-2* inhibitor in cats. It has not been established if the specificity for *COX-1* or *COX-2* is related to efficacy or safety. Deracoxib has a half-life of 3 hours in dogs at 2-3 mg/kg and 19 hours at 20 mg/kg. It is highly protein bound. Oral absorption is 90% in dogs. Feeding delays absorption but does not diminish overall absorption. In cats, the half-life is approximately 8 hours.

## Indications and Clinical Uses

Deracoxib is used to decrease pain, inflammation, and fever. It has been used for the acute and chronic treatment of pain and inflammation in dogs. One of the most common uses is osteoarthritis, but it also has been used for pain associated with surgery. There has been only limited use of deracoxib in horses, and administration to other large animals has not been reported. Deracoxib, like other *COX-2* inhibitors, may have some antitumor properties. It has produced beneficial effects in dogs with transitional cell carcinoma.

## Precautionary Information

### Adverse Reactions and Side Effects

Gastrointestinal problems are the most common adverse effects associated with NSAIDs and can include vomiting, diarrhea, nausea, ulcers, and erosions of the GI tract. Gastric and duodenal ulcers have been reported from use of deracoxib in dogs. In field trials with deracoxib, vomiting was the most often reported adverse effect. Renal toxicity, especially in dehydrated animals or animals with preexisting renal disease, has been shown for some NSAIDs. In studies performed in dogs, higher doses (five times the dose) caused azotemia in normal dogs.

**Contraindications and Precautions**

Dogs and cats with preexisting GI or renal problems may be at a greater risk of adverse effects from NSAIDs. Safety in pregnancy is not known, but adverse effects have not been reported. Safety studies are not available for dogs <4 months of age, pregnant animals, or lactating animals. In cats, use only as a single dose.

**Drug Interactions**

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

**Instructions for Use**

Chewable tablets can be administered with or without food. Long-term studies have not been completed in cats; only single-dose studies have been reported.

**Patient Monitoring and Laboratory Tests**

Monitor GI signs for evidence of diarrhea, GI bleeding, or ulcers. Because of risk of renal injury, monitor renal parameters (water consumption, blood urea nitrogen [BUN], creatinine, and urine-specific gravity) periodically during treatment. Deracoxib does not appear to affect thyroid hormone assays in dogs.

**Formulations**

- Deracoxib is available in 25-, 75-, and 100-mg chewable tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Deracoxib has been mixed in a liquid suspension in water. However, stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- Postoperative pain: 3-4 mg/kg once daily as needed for up to 7 days.  
Chronic use: 1-2 mg/kg once daily PO.

**Cats**

- 1 mg/kg single dose, PO.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

Do not administer to animals that produce food.

RCI Classification: 4

**Desmopressin Acetate**

dess-moe-press'in ass'ih-tate

**Trade and other names:** DDAVP

**Functional classification:** Hormone

## Pharmacology and Mechanism of Action

Synthetic peptide similar to antidiuretic hormone (ADH). It produces similar effects as natural ADH and is used to treat diabetes insipidus (DI) in animals. This action is related to stimulation of permeability to water to increase water reabsorption in the distal renal tubule. The difference between DDAVP and natural ADH is that DDAVP is longer acting and produces fewer vasoconstriction effects. In addition to the hormone effects, in humans, administration of DDAVP results in a twofold to fivefold increase in the plasma von Willebrand factor. It may induce a 50% increase in von Willebrand factor in some animals, but not as consistently as when administered to people.

## Indications and Clinical Uses

Desmopressin is used as replacement therapy for patients with DI and has been used for treatment of patients with mild to moderate von Willebrand's disease prior to surgery or another procedure that may cause bleeding. However, the response in von Willebrand-deficient dogs is not as consistent or as great as in people.

### Precautionary Information

#### Adverse Reactions and Side Effects

No side effects reported. In people, it has rarely caused thrombotic events.

#### Contraindications and Precautions

There are no specific contraindications.

#### Drug Interactions

Administration of urea and fludrocortisone will increase the antidiuretic effects.

## Instructions for Use

Desmopressin is used only for central forms of DI. Duration of effect is variable (8-20 hours) but typically has a duration of 8-12 hours. It is ineffective for treatment of nephrogenic DI or polyuria from other causes. Intranasal product has been administered as eye drops in dogs. Onset of effect is within 1 hour. Oral tablets are available for humans, but the effects in dogs have not been reported.

## Patient Monitoring and Laboratory Tests

Monitor water intake and urinalysis to assess therapy. Desmopressin may be used as a test for DI in animals. To perform this test, administer 2 mcg/kg SQ or IV or 20 mcg intranasally or in the eye. This should be followed by monitoring of urine concentration and the animal's body weight. Increase in urine-concentrating ability may indicate a diagnosis of DI.

## Formulations

- Desmopressin is available in a 4-mcg/mL injection, acetate nasal solution 100-mcg/mL (0.01%) metered spray, and 0.1- and 0.2-mg tablets (scored).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

- DI: 2-4 drops (2 mcg) q12-24h intranasally or in eye. Alternatively, 0.5-2 mcg/dog q12-24h IV or SQ.
- Oral Dose: 0.05-0.1 mcg/kg q12h, or as needed. The oral dose may be increased to 0.1-0.2 mcg/kg as needed. Alternatively, administer 0.1 mg (total dose) per dog, PO, three times daily and adjust dose to control clinical signs (polyuria and polydipsia). If this dose is successful, decrease frequency to twice daily.



## 214 Desoxycorticosterone Pivalate

- von Willebrand's disease treatment: 1 mcg/kg (0.01 mL/kg), administered SQ or diluted in 20 mL of saline and administered over 10 min IV.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Withdrawal times are not established. However, this drug has rapid clearance, with little risk from residues; therefore a short withdrawal time is suggested for food animals.

## Desoxycorticosterone Pivalate

dess-oks-ih-kor-tik-oh-steer'one piv'ah-late

**Trade and other names:** Percorten-V, DOCP, and DOCA pivalate

**Functional classification:** Corticosteroid

### Pharmacology and Mechanism of Action

Mineralocorticoid with no glucocorticoid activity. Desoxycorticosterone mimics the effects of aldosterone by retaining sodium. The pivalate formulation is absorbed slowly and produces a long-lasting effect from a single administration.

### Indications and Clinical Uses

Desoxycorticosterone is used for adrenocortico insufficiency (hypoadrenocorticism). Some dogs also may require concurrent glucocorticosteroid therapy when it is used to treat insufficiency.

### Precautionary Information

#### Adverse Reactions and Side Effects

Excessive mineralocorticoid effects are possible with high doses. Signs of iatrogenic hyperadrenocorticism are not expected with this drug.

#### Contraindications and Precautions

Do not use in pregnant animals. It must be used cautiously in patients with congestive heart failure or renal disease. Dogs with congestive heart failure may have exacerbation of clinical signs from treatment with DOCP. In those cases, reduce dose (by one-half for example).

#### Drug Interactions

Aldosterone antagonists (spironolactone) will blunt the effect.

### Instructions for Use

Initial dose based on average response in clinical patients, but individual doses may be based on monitoring electrolytes in patients. The actual interval between doses may range from 14 to 35 days.

### Patient Monitoring and Laboratory Tests

Monitor serum sodium and potassium.

### Formulations

- Desoxycorticosterone is available in 25-mg/mL suspension for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 1.5-2.2 mg/kg q25 days IM. Adjust dose by monitoring electrolytes. DOCP also has been effective in dogs when administered 2.2 mg/kg SQ, once per 25 days.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established. However, because of low risk of residues, no withdrawal times are suggested.

RCI Classification: 4

## Detomidine Hydrochloride

deh-toe'mih-deen hye-droe-klor'ide

**Trade and other names:** Dormosedan, Dormosedan Gel

**Functional classification:** Alpha<sub>2</sub> analgesic

## Pharmacology and Mechanism of Action

Alpha<sub>2</sub> adrenergic agonist. Alpha<sub>2</sub> agonists decrease release of neurotransmitters from the neuron. The proposed mechanism whereby they decrease transmission is via binding to presynaptic alpha<sub>2</sub> receptors (negative feedback receptors). The result is decreased sympathetic outflow, analgesia, sedation, and anesthesia. Detomidine gel is absorbed from the oral mucous membrane with bioavailability in horses of 22%. Other drugs in this class include xylazine, dexmedetomidine, medetomidine, romifidine, and clonidine. In dogs, the half-life from IV administration is approximately 30 minutes, with a volume of distribution of 0.6 L/kg. After application of the mucosal gel to dogs, the peak occurred at 1 hours, the half-life was 40 minutes, and absorption was 34%. In horses, the half-life of the oral mucosal gel was 1.5 hours and was below the detection limit in plasma by 24 hours.

## Indications and Clinical Uses

Detomidine is used primarily as a sedative, anesthetic adjunct, and analgesia. It is used in horses more often than in other species. When used to treat pain from colic in horses, the duration of effect is approximately 3 hours (20 or 40 mcg/kg). Detomidine also has been administered for epidural analgesia. For pain, detomidine appears to be more potent and longer acting than xylazine. Detomidine in the gel form (Dormosedan Gel) for horses is administered orally to produce mucosal absorption. It is indicated for producing minor standing sedation to facilitate minor procedures (shoeing, clipping, trimming) or calming a fractious horse. Onset of action is 40 minutes and duration is 90-180 minutes.

## Precautionary Information

### Adverse Reactions and Side Effects

At typical doses, sedation, ataxia, swaying, sweating, and bradycardia are common. Cardiac depression, atrioventricular (AV) block, and hypotension are possible with high doses. In some horses, hyperresponsiveness to stimuli occurs. Diuresis occurs as a consequence of the hyperglycemia produced by alpha<sub>2</sub> agonists such

as detomidine. Yohimbine (0.11 mg/kg) can be used to reverse effects of  $\alpha_2$  agonists such as detomidine. In small animals, atipamezole also can be used to reverse effects from detomidine.

### **Contraindications and Precautions**

Concurrent use of detomidine with sulfonamides IV can lead to cardiac arrhythmias. Xylazine causes problems in pregnant animals, and this also should be considered for other  $\alpha_2$  agonists. Use cautiously in animals that are pregnant because it may induce labor. In addition, it may decrease oxygen delivery to a fetus in late gestation. Detomidine gel can be absorbed across the skin and from eye and mouth contact in humans. If there is accidental exposure, immediately rinse with soap and water. Contact a physician if there are other concerns.

### **Drug Interactions**

Other drugs that depress the heart may increase risk for arrhythmias.

## **Instructions for Use**

It is used primarily for horses, and although not approved for small animals, dosages are listed later. Atropine (0.01 to 0.02 mg/kg) has been used to prevent bradycardia, but is not necessary for routine use. It may be administered with other anesthetics, analgesics, and sedatives (including butorphanol), and benzodiazepines.

## **Patient Monitoring and Laboratory Tests**

Monitor heart rate and, if possible, the electrocardiogram (ECG) during treatment with this class of drugs. If available, blood pressure monitoring may be indicated in some patients.

## **Formulations**

- Detomidine is available in a 10-mg/mL injection. Oral gel is 7.6 mg/mL in a 3-mL syringe.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## **Small Animal Dosage**

### **Dogs**

- 5 mcg/kg IV or 10-20 mcg/kg IM.
- Oral mucosal application: mild sedation 0.5 mg/m<sup>2</sup>; higher sedation and lateral recumbency: 1.0 mg/m<sup>2</sup>. (Average dose is 35 mcg/kg.) A high dose of 2-4 mg/m<sup>2</sup> will produce more profound sedation. The gel is applied to the upper gingiva of dogs, (approximately 0.1 mL). Reversal with 0.1 mg/kg atipamezole IM.

### **Cats**

- Oral (transmucosal): 0.5 mg/kg. Administer with ketamine (10 mg/kg) by spraying into cat's mouth.
- Oral (transmucosal): for greater sedation use 2-4 mg/m<sup>2</sup> (anticipate vomiting at this dose). Reversal with 0.1 mg/kg atipamezole IM.

## **Large Animal Dosage**

### **Horses**

*(Dose of 10-20 mcg/kg is equivalent to 5-10 mg per horse)*

- Sedation: 20-40 mcg/kg (0.02-0.04 mg/kg) IV or IM. Lower doses of 10-20 mcg/kg are sometimes used in practice initially, then repeated as needed. For example, doses of 10 mcg/kg (0.01 mg/kg) will produce slightly less ataxia and sedation. Doses as low as 5 mcg/kg have been used in draft horses.

- Analgesia: 20 mcg/kg (0.02 mg/kg) IV or IM. Duration of analgesia may be longer if a dose of 40 mcg/kg is used.
- Constant-rate infusion (CRI): 10 mcg/kg bolus IV, followed by 0.5 mcg/kg/min for 15 min, then progressively decreasing the rate as needed to 0.1 mcg/kg/min.
- Oral mucosal: 40 mcg/kg (approximately 2.5 mL to a 1000 pound horse) administered sublingually.

#### Cattle

- 2-10 mcg/kg (0.002-0.1 mg/kg) IV or 5-40 mcg/kg (0.005-0.04 mg/kg) IM.

#### Calves

- 30 mcg/kg, IV, or Detomidine oral mucosal gel (equine formulation): 80 mcg/kg

### Regulatory Information

Cattle withdrawal times (extralabel): 3 days meat; 72 hours milk.

RCI Classification: 3

## Dexamethasone

deks-ah-meth'ah-sone

**Trade and other names:** Azium solution in polyethylene glycol, DexaJect, Dexavet, Decadron, Dexasone, Voren suspension, and generic brands

**Functional classification:** Corticosteroid

### Pharmacology and Mechanism of Action

Corticosteroid. Anti-inflammatory and immunosuppressive effects of dexamethasone are approximately 30 times more potent than cortisol. Anti-inflammatory effects are complex, but primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. Use is for treatment of inflammatory and immune-mediated disease. This dexamethasone solution differs from dexamethasone sodium phosphate in that the sodium phosphate form is water soluble and appropriate for IV administration. Dexamethasone solution is in a polyethylene glycol vehicle that should not be administered rapidly IV. Dexamethasone-21-isonicotinate is a suspension registered for IM use. After an injection of 10 mg (total dose) to horses, the half-life was 2.5-5 hours, and the volume of distribution (VD<sub>ss</sub>) was 1.7 L/kg. Oral administration of the same dose had a half-life of 4.3 hours and bioavailability (F) of 61%, with a peak concentration at 1.3 hours. The suspension, (dexamethasone-21-isonicotinate) has a slow-release and produces a 39 hour half-life in horses and suppresses cortisol for 140 hours.

### Indications and Clinical Uses

Dexamethasone is used for treatment of inflammatory and immune-mediated disease. The use of dexamethasone at high doses for treatment of shock is controversial. Most recent evidence does not support administration of dexamethasone for this use. Dexamethasone is also used as a diagnostic test of adrenal function. Large animal uses include induction of parturition (cattle) and treatment of inflammatory conditions. In cattle, corticosteroids also have been used in the treatment of ketosis. In horses, dexamethasone has been used to treat recurrent airway obstruction (RAO).

### Precautionary Information

#### Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic-pituitary-adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone,

decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include infections from Demodex, toxoplasmosis, fungal infections, and urinary tract infections (UTIs). High-dose glucocorticoids in animals with neurologic disease can lead to excitotoxic cell death and oxidative injury via increased excitatory amino acids. In horses, dexamethasone adverse effects include risk of laminitis, although this effect is controversial and not supported by strong evidence.

### **Contraindications and Precautions**

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously in animals with diabetes or renal failure and in pregnant animals. Intravenous injections should be done slowly because formulations contain polyethylene glycol, which can cause reactions from rapid IV injection (hemolysis, hypotension, and collapse). Do not administer dexamethasone-21-isonicotinate IV (IM use only).

### **Drug Interactions**

Administration of corticosteroids with NSAIDs will increase the risk of GI injury. pH is 7-8.5. Do not mix with acidifying solutions. Otherwise, it is compatible with most IV fluid solutions.

## **Instructions for Use**

Dosing schedules are based on the condition treated. Anti-inflammatory effects occur at doses of 0.1-0.2 mg/kg, and immunosuppressive effects occur at 0.2-0.5 mg/kg. Dexamethasone is used to test for hyperadrenocorticism. For the low-dose dexamethasone suppression test: dogs 0.01 mg/kg (or 0.015 mg/kg in some references) IV and cats 0.1 mg/kg IV; collect sample at 0, 4, and 8 hours. For high-dose dexamethasone suppression test: dogs 0.1 mg/kg (or 1.0 mg/kg in some references) and cats: 1.0 mg/kg. In horses, oral absorption is higher in unfed horses. Oral absorption from powder is higher than with solution.

## **Patient Monitoring and Laboratory Tests**

For the low-dose and high-dose dexamethasone suppression tests, administer either 0.01 or 0.1 mg/kg and collect cortisol sample at 0, 4, and 8 hours after administration. The normal cortisol concentration after suppression test should be <30-40 nmol/L (1.1-1.3 mcg/dL). For the dexamethasone suppression test for horses, administer 0.04 mg/kg IM and collect postcortisol sample 24 hours later. Normal suppression in horses is <1 mcg/dL.

## **Formulations**

- Dexamethasone is available in a 2-mg/mL solution, which contains 500 mg polyethylene glycol; 0.25-, 0.5-, 0.75-, 1-, 1.5-, 2-, 4-, and 6-mg tablets; 0.1- and 1-mg/mL oral solution; and 10 mg per 15 g powder. Dexamethasone-21-isonicotinate slow-release suspension in an aqueous vehicle is 1 mg/mL.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Dexamethasone formulated in various oral mixtures to enhance flavoring was stable for 26 weeks at room temperature or refrigerated. Dexamethasone sodium phosphate is freely soluble in water, but dexamethasone solution (in polyethylene glycol) is practically insoluble in water.

## **Small Animal Dosage**

### **Dogs and Cats**

- Anti-inflammatory: 0.07-0.15 mg/kg q12-24h IV, IM, or PO. (Higher dose of 0.15 mg/kg is typical for cats.)

- Immunosuppressive: 0.125-0.25 mg/kg q24h, IV, IM, or PO for initial treatment.
- Pulse dose: 0.5 mg/kg PO, for 4 consecutive days, then repeated every 28 days.
- Oral dose (cats): 0.1-0.2 mg/kg q24h, PO, added to food. After initial dose, lower dose to maintenance of 0.05 mg/kg q48-72h, PO.
- Low-dose dexamethasone suppression test: 0.01 mg/kg IV (dog) and 0.1 mg/kg IV (cat).
- High-dose dexamethasone suppression test: 0.1 mg/kg IV (dog) and 1.0 mg/kg IV (cat).
- Dexamethasone-21-isonicotinate: 0.03-0.05 mg/kg IM.

## Large Animal Dosage

### Cattle and Horses

- 0.04-0.15 mg/kg per day IV or IM. Some product labeling lists a total dose of 5-20 mg/animal, which corresponds to 0.01 to 0.04 mg/kg/day. However, for some conditions, higher doses may be needed.
- Horses, treatment of RAO: 0.05-0.1 mg/kg IV or IM q24h, or 0.165 mg/kg PO q24h, usually for 2-3 days, but oral treatment has been continued for 7 days, then tapered to half the dose for another 7 days.
- Induction of parturition (cattle): 0.05 mg/kg (25 mg/animal) as a single dose during the last week or 2 weeks of pregnancy. A dose of prostaglandin PG-F<sub>2</sub> alpha may be administered concurrently (0.5 mg/animal).
- Dexamethasone-21-isonicotinate: 0.01-0.04 mg/kg IM.

### Sheep

- Induction of parturition: 0.15 mg/kg/day IM for 1-5 days during the last week of gestation.

## Regulatory Information

Dexamethasone is approved for use in cattle, but withdrawal times are not established. Although withdrawal times are not listed on the label, at least 96 hours should be used for milk and 4-8 days for meat. Allow at least 3 weeks to eliminate residues from kidney and liver and 6 weeks to deplete drug from IM injection site. RCI Classification: 4

## Dexamethasone Sodium Phosphate

**Trade and other names:** Sodium phosphate: DexaJect SP, Dexavet, and Dexasone. Decadron and generic brand tablets

**Functional classification:** Corticosteroid

## Pharmacology and Mechanism of Action

Corticosteroid. Anti-inflammatory and immunosuppressive effects are approximately 30 times more potent than cortisol. Anti-inflammatory effects are complex, but primarily occur via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. The difference among formulations is that dexamethasone sodium phosphate is a water-soluble formulation that can be injected intravenously. Dexamethasone solution is in a polyethylene glycol vehicle that should not be administered rapidly intravenously. Half-life in plasma for dexamethasone ranges from 3-6 hours, but duration of action is 36-48 hours.

## Indications and Clinical Uses

Use of dexamethasone is for treatment of inflammatory and immune-mediated disease. The use of dexamethasone at high doses for treatment of shock is controversial. Most

recent evidence does not support administration of dexamethasone for this use. Large animal uses include induction of parturition (cattle) and treatment of inflammatory conditions. In cattle, corticosteroids also have been used in the treatment of ketosis.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and HPA axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include Demodex, toxoplasmosis, fungal infections, and UTIs. In horses, additional adverse effects include risk of laminitis.

#### **Contraindications and Precautions**

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously, or not at all, in animals receiving NSAIDs because these drugs administered concurrently will increase the risk of GI ulceration. Use cautiously in animals with diabetes or renal failure and in pregnant animals.

#### **Drug Interactions**

Administration of corticosteroids with NSAIDs will increase the risk of GI injury.

### **Instructions for Use**

Dosing schedules are based on desired effect. Anti-inflammatory effects are seen at doses of 0.1-0.2 mg/kg, and immunosuppressive effects are seen at 0.2-0.5 mg/kg. Dexamethasone is used for testing hyperadrenocorticism. For the low-dose dexamethasone suppression test (for dogs), use 0.01 mg/kg (or 0.015 mg/kg in some references) IV and 0.1 mg/kg IV (for cats). For the high-dose dexamethasone suppression test in dogs, use 0.1 mg/kg (or 1.0 mg/kg in some references) and in cats, use 1.0 mg/kg. For the test in horses, administer 40 mcg/kg.

### **Patient Monitoring and Laboratory Tests**

Monitor CBC periodically during treatment to assess effects. For monitoring a low-dose dexamethasone suppression test, collect samples at 4 and 8 hours after dexamethasone. A normal suppression test should be cortisol <30-40 nmol/L (1.1-1.4 mcg/dL). For dexamethasone suppression in horses, collect samples at 17 and 19 hours. Normal horses should have cortisol <1.0 mcg/dL.

### **Formulations**

- Sodium phosphate solution is available as 4 mg/mL, equivalent to 3 mg/mL of dexamethasone base.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Dexamethasone sodium phosphate in other aqueous solutions has been stable for 28 days. Dexamethasone sodium phosphate is freely soluble in water, but dexamethasone solution (in polyethylene glycol) is practically insoluble in water. If dexamethasone sodium phosphate is mixed with 5% dextrose solution or saline, it is stable for 24 hours.

### **Small Animal Dosage**

#### **Dogs and Cats**

- Anti-inflammatory: 0.07-0.15 mg/kg q12-24h IV or IM.
- Shock, spinal injury (efficacy in question): 2.2-4.4 mg/kg IV.

- Low-dose dexamethasone suppression test: 0.01 mg/kg or 0.015 mg/kg IV (for dogs) and 0.1 mg/kg IV (for cats) and collect sample at 0, 4, and 8 hours.
- High-dose dexamethasone suppression test: 0.1 mg/kg or 1.0 mg/kg IV (for dogs) and 1.0 mg/kg IV (for cats).

## Large Animal Dosage

### Cattle and Horses

- Treatment of inflammation: 0.04-0.15 mg/kg/day IV or IM.
- Ketosis (cattle): 0.01 to 0.04 mg/kg IV or IM.
- Induction of parturition (cattle): 0.05 mg/kg (25 mg per animal) as a single dose during the last week or 2 weeks of pregnancy. A dose of prostaglandin PG-F<sub>2</sub> alpha may be administered concurrently (0.5 mg/animal).
- Dexamethasone suppression test in horses: 40 mcg/kg and collect samples at 17 and 19 hours.

### Sheep

- Induction of parturition: 0.15 mg/kg/day IM for 1-5 days during the last week of gestation.

## Regulatory Information

Although withdrawal times are not established, at least 96 hours is required for milk and 4-8 days for meat. However, at least 3 weeks are required to eliminate residues from kidney and liver and 6 weeks for IM injection site.

## Dexmedetomidine Hydrochloride

dex-meh-deh-toe'mih-deen hye-droe-klor'ide

**Trade and other names:** Dexdomitor

**Functional classification:** Analgesic, alpha<sub>2</sub> agonist

## Pharmacology and Mechanism of Action

Alpha<sub>2</sub>-adrenergic agonist. Alpha<sub>2</sub> agonists decrease release of neurotransmitters from the neuron. Dexmedetomidine and medetomidine (Domitor) are very similar in activity. Medetomidine is a racemic mixture containing 50% dexmedetomidine and 50% levomedetomidine. Dexmedetomidine is the active enantiomer of the mixture (D-isomer); therefore (on a mg/mg basis) dexmedetomidine is twice the potency of medetomidine but with the same pharmacological activity and equivalent analgesic and sedative effects. The proposed mechanism whereby they decrease transmission is via binding to presynaptic alpha<sub>2</sub> receptors (negative feedback receptors). The result is decreased sympathetic outflow, analgesia, sedation, and anesthesia. Other drugs in this class include medetomidine, xylazine, detomidine, romifidine, and clonidine. Receptor-binding studies indicate that alpha<sub>2</sub>/alpha<sub>1</sub>-adrenergic receptor selectivity is more than 10 times that of xylazine. The pharmacokinetics have been studied in several species. In horses the half-life is only 8 minutes with a rapid clearance and volume of distribution of over 1 L/kg.

## Indications and Clinical Uses

Dexmedetomidine, like other alpha<sub>2</sub> agonists, is used as a sedative, anesthetic adjunct, and analgesia. It is approved for use in both dogs and cats. It can be administered to facilitate examinations, diagnostic procedures, treatments, ear and teeth cleaning, and minor surgery. It has been used to sedate animals for intradermal skin testing without affecting results. In cats, the peak effects are observed in 15-60 minutes, and the



recovery occurs by 180 minutes. It has similar clinical effects as medetomidine and can be used for similar indications. It can be administered in combination with ketamine, butorphanol, or opiate agonists for sedation and short-term surgical procedures (see “[Instructions for Use](#)”). Dexmedetomidine is well absorbed across membranes and has produced similar effects in cats after oral transmucosal (buccal) administration compared to IM injection. In the dosing section, note that many doses listed are lower than the manufacturer’s approved label dose.

## **Precautionary Information**

### **Adverse Reactions and Side Effects**

In small animals, vomiting is the most common acute effect. Vomiting is more common in cats than dogs. Alpha<sub>2</sub> agonists decrease sympathetic output. Cardiovascular depression may occur. Like medetomidine, dexmedetomidine can produce an initial bradycardia and hypertension. An initial increase in blood pressure may be followed by a decrease in blood pressure caused by decreased sympathetic tone. Lower respiratory rate and body temperature occur in animals during dexmedetomidine sedation. Transient arrhythmias may occur in some animals. Paradoxical excitement may occur in some animals, and animals with high anxiety levels may not respond predictably to alpha<sub>2</sub> agonists. If adverse reactions are observed, reverse with atipamezole (Antisedan). Yohimbine also can reverse medetomidine. It is not recommended to administer atropine to animals to modify cardiovascular effects. Administration of atropine to dogs with dexmedetomidine resulted in increases in blood pressure and heart rate and deleterious cardiac arrhythmias. In horses, there are prominent sedative effects, especially in the first 20-30 minutes and decreased intestinal motility that lasted 60 minutes.

### **Contraindications and Precautions**

Use cautiously in animals with heart disease. Use may be contraindicated in older animals with preexisting cardiac disease. Use cautiously in animals with respiratory, liver, or kidney disease. Do not use in animals with signs of shock. Xylazine causes problems in pregnant animals, and this also should be considered for other alpha<sub>2</sub> agonists. Use cautiously in animals that are pregnant because it may induce labor. In addition, it may decrease oxygen delivery to fetus in late gestation. Dexmedetomidine can be absorbed through intact human skin; therefore avoid human exposure.

### **Drug Interactions**

Do not use with other drugs that may cause cardiac depression. Do not mix in vial or syringe with other anesthetics. Reverse with atipamezole at a dose of 25-300 mcg/kg IM. Use with opioid analgesic drugs will greatly enhance the CNS depression. Consider lowering doses if administered with opioids. Anticholinergic drugs (e.g., atropine) may be given in moderate doses *prior* to drug administration to prevent bradycardia induced by alpha<sub>2</sub> agonists, but it is not routinely needed and may prolong initial hypertension. However, administration *simultaneously* with alpha<sub>2</sub> agonists is not recommended. Administration of atropine to dogs with dexmedetomidine resulted in adverse cardiovascular effects.

## **Instructions for Use**

Dexmedetomidine, medetomidine, and detomidine are more specific for the alpha<sub>2</sub> receptor than xylazine. They may be used for sedation, analgesia, and minor surgical procedures. It is recommended to withhold food for several hours prior to administration of alpha<sub>2</sub> agonists to minimize vomiting. Lower doses are often administered for cases when less sedation is needed or when combined with other drugs. Dexmedetomidine can be used with other anesthetics such as propofol, ketamine, thiopental, opiates,

benzodiazepines, and inhalent gas anesthetics. However, lower doses (as much as 40%-60%) of other drugs are anticipated when used with dexmedetomidine. When administered at a dose of 10 mcg/kg to cats in combination with butorphanol or ketamine, there was adequate sedation without significant cardiovascular effects. It has also been safe and effective in cats as a preanesthetic at a dose of 40 mcg/kg combined with 5 mg/kg ketamine. In dogs and cats, reverse with atipamezole at a dose of 25-300 mcg/kg (equal to volume of dexmedetomidine used) IM.

### Patient Monitoring and Laboratory Tests

Monitor vital signs during anesthesia. Monitor heart rate, blood pressure, and ECG during anesthesia. Alpha<sub>2</sub> agonists will increase blood glucose because of effects on insulin secretion.

### Formulations

- Dexmedetomidine is available in vials containing 0.5 mg/mL injection, and a lower concentration of 0.1 mg/mL in sterile vials. Human formulation is Precedex.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 125 mcg/m<sup>2</sup> IM for preanesthetic, minor sedation, short-term procedures, and analgesia (range is 9 mcg/kg for small dogs to 3 mcg/kg for large dogs).
- 375 mcg/m<sup>2</sup> IV or 500 mcg/m<sup>2</sup> IM for deeper sedation, analgesia, and minor surgical procedures. The per body weight dose range is 17.6 mcg/kg IV, and 23.5 mcg/kg IM, for 10 kg dogs; and, 10.6 mcg/kg IV and 14 mcg/kg IM, for 46 kg dogs.
- Lower doses are used for short-term sedation and analgesia or when combined with other analgesic or anesthetic agents.
- Combination: Ketamine (3 mg/kg), dexmedetomidine (15 mcg/kg), and buprenorphine (40 mcg/kg) can be combined for one single IM injection in dogs for short-term surgical procedure or intubation for surgery.

#### Cats

- 40 mcg/kg (0.04 mg/kg) IM (0.35 mL for 4-kg cat). Oral transmucosal administration at this dose produces equivalent effects as IM injection. IV dose is 5-20 mcg/kg. Reverse with atipamezole 0.2 mg/kg IM (may be used with ketamine 5 mg/kg).
- Lower doses (e.g., 10-25 mcg/kg) have been used for short-term sedation and analgesia or when combined with other agents.
- These combinations (e.g., 3 mg/kg ketamine + 25 mcg/kg dexmedetomidine) can be combined in one syringe and administered IM 10 minutes prior to a minor surgical procedure.

### Large Animal Dosage

#### Horses

- 5 mcg/kg IV bolus. Constant rate infusion: 8 mcg/kg per hour, IV

### Regulatory Information

Withdrawal times are not established for animals that produce food. The withdrawal time for xylazine in food animals is 4 days for meat and 24 hours for milk. A minimum of those withdrawal periods should be used for dexmedetomidine. For additional extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Dextran

deks'tran

**Trade and other names:** Dextran 70 and Gentran-70**Functional classification:** Fluid replacement

### Pharmacology and Mechanism of Action

Synthetic colloid used for volume expansion. Dextran is a glucose polymer and is available as low molecular weight (Dextran 40) and high molecular weight (Dextran 70). Dextran 70 is the most often used. The colloids such as dextrans are large-molecular-weight molecules that remain in the vasculature because of their large size. Therefore they increase colloid osmotic pressure within the vasculature to prevent intravascular fluid loss and inhibit tissue edema. Other colloids used are hetastarch and pentastarch.

### Indications and Clinical Uses

Dextran is a high-molecular-weight compound administered IV to maintain intravascular volume. It is used for acute treatment of hypovolemia and shock. Duration of effect is approximately 24 hours.

### Precautionary Information

#### Adverse Reactions and Side Effects

There is only limited use in veterinary medicine, and adverse effects have not been reported. In people, coagulopathies are possible because of decreased platelet function and antithrombotic effects. Acute renal failure has occurred, and anaphylactic shock also has occurred in people.

#### Contraindications and Precautions

Do not use in animals that are prone to bleeding problems. Dextrans can interfere with cross-matching of blood for transfusion. Cats are more susceptible to fluid overload than dogs, and lower doses must be used in cats.

#### Drug Interactions

Compatible with most IV fluid solutions, including 0.9% saline solution and 5% dextrose solution.

### Instructions for Use

Used primarily in critical care situations. Delivered slowly via CRI (60-90 minutes). In emergency use, bolus doses of 20 mL/kg can be administered more rapidly.

### Patient Monitoring and Laboratory Tests

Monitor patient's cardiopulmonary status carefully during administration. Dextrans can interfere with cross-matching of blood.

### Formulations

- Dextran is available in 250-, 500-, and 1000-mL solution for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 10-20 mL/kg/day IV to effect, usually administered over 30-60 minutes.

### Cats

- 5-10 mL/kg/day IV, over 30-60 minutes.

## Large Animal Dosage

### Horses and Cattle

- 10 mL/kg/day IV.

## Regulatory Information

Withdrawal times are not established. However, this drug presents little risk from residues; therefore a short withdrawal time is suggested for animals intended for food.

## Dextromethorphan

deks-troe-meth-or'fan

**Trade and other names:** Benylin and others

**Functional classification:** Antitussive

## Pharmacology and Mechanism of Action

Centrally acting antitussive drug. Dextromethorphan shares similar chemical structure to opiates, but does not affect opiate receptors and appears to directly affect cough receptor. Dextromethorphan is the d-isomer of levorphan (the l-isomer of levorphan is an opiate with addictive properties, but the d-isomer is not). Dextromethorphan produces mild analgesia and modulates pain via its ability to act as an n-methyl D-aspartate (NMDA) antagonist, but this is unrelated to the antitussive action.

## Indications and Clinical Uses

Dextromethorphan has been used for suppression of nonproductive cough. However, its efficacy for reducing cough has been questioned because of a lack of proof. Dextromethorphan also has been used as an adjunct for treating pain because of NMDA antagonism. Pharmacokinetic studies in dogs indicated that dextromethorphan does not attain effective concentrations after oral administration. Even after IV administration, concentrations of the parent drug and active metabolite persisted for only a short time after dosing. Therefore routine use in dogs is not recommended until more data are available to establish safe and effective doses. Data have not been reported for the pharmacokinetics in cats or any other species.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are not reported in veterinary medicine. High overdose may cause sedation. After administration to dogs, dextromethorphan produced adverse effects seen as vomiting after oral doses and CNS reactions after IV administration. Some preparations contain alcohol, which can be unpalatable in small animals, especially cats.

### Contraindications and Precautions

There are no contraindications identified for animals. However, pet owners should be cautioned that many over-the-counter (OTC) preparations contain other drugs that may produce significant side effects. For example, some combinations also contain acetaminophen, which can be toxic to cats. Some preparations also contain a decongestant, such as pseudoephedrine, which can cause excitement and other side effects.

**Drug Interactions**

There are no direct interactions identified for dogs. However, interactions are possible when used with other drugs that may interfere with cytochrome P450 metabolism.

**Instructions for Use**

Many OTC preparations may contain other ingredients (e.g., antihistamines, decongestants, ibuprofen, and acetaminophen). Adverse effects from each of these ingredients, such as toxic reactions caused by acetaminophen, CNS excitement from decongestants, and GI toxicity from ibuprofen, can occur in animals.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Dextromethorphan is available in syrup, capsules, and tablets in many OTC products. Many preparations are available without a prescription in liquid and tablet form. Over-the-counter formulations may vary in concentration, but typically contain 2, 5, 10, or 15 mg/mL and in 15-20-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs and Cats**

- 0.5-2 mg/kg q6-8h PO (however, use is not recommended because efficacy at these doses has not been shown).

**Large Animal Dosage**

- No dosing information available. It has little value for treating large animals.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

**Dextrose Solution**

deks'troze

**Trade and other names:** D5W

**Functional classification:** Fluid replacement

**Pharmacology and Mechanism of Action**

Dextrose is a sugar added to fluid solutions. It is isotonic as delivered. Five percent dextrose contains 50 g of dextrose per liter. The pH of this solution is 3.5-6.5. Alternatively, 50% dextrose solution can be added to IV fluids to supplement dextrose. For example, 100 mL of 50% dextrose added to 1000 mL supplies 5% dextrose.

**Indications and Clinical Uses**

Five percent dextrose is an isotonic fluid solution used for IV administration. Dextrose is considered only for short-term use because it is deficient in electrolytes. After the

glucose is metabolized, the water is rapidly distributed out of the vascular space. For emergency treatment of hypoglycemia or to supplement fluids, a 50% dextrose solution (500 mg/mL) is used. Dextrose has been administered in a 50% solution to treat periparturient cows with ketosis and hepatic lipidosis or to support anorexic or recumbent cows. However there is no established benefit of 50% dextrose treatment for prevention of ketosis in dairy cattle as a single treatment of 0.5L or 1.0L IV.

### Precautionary Information

#### Adverse Reactions and Side Effects

High doses can produce pulmonary edema.

#### Contraindications and Precautions

Use cautiously in animals with low electrolyte concentrations. Five percent dextrose solution is not a suitable maintenance solution because it does not provide electrolytes. It should not be considered as a replacement solution or a source of energy requirements; it supplies only 170 kcal/L. When aggressive treatment is used with 50% dextrose, it may cause rapid decrease in plasma phosphorous and potassium (intracellular shift).

#### Drug Interactions

No interactions. Five percent dextrose solution is compatible with fluids and most IV drugs.

### Instructions for Use

Dextrose is a commonly used fluid solution administered via CRI. However, it is not a maintenance solution. Dextrose 50% solution can also be added to fluids to supply dextrose. For example, 50 mL of 50% dextrose is added to 1000 mL fluids to achieve a final 2.5% solution.

### Patient Monitoring and Laboratory Tests

Monitor patient's hydration status and evidence of pulmonary edema during infusion. Monitor acid-base status.

### Formulations

- Fluid solution for IV administration is 5% dextrose, which contains 5 g of glucose per 100 mL (50 g/L). Fifty percent dextrose contains 500 mg/mL (50 g/100 mL).

### Stability and Storage

Store in a tightly sealed container at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- Five percent dextrose solution: 40-50 mL/kg q24h IV.
- In emergency hypoglycemic crisis: 1 mL 50% dextrose solution IV diluted with saline.

### Large Animal Dosage

#### Calves, Cattle, and Horses

- Five percent dextrose solution: 45 mL/kg q24h IV.
- Cows: 0.1-0.2 gm/kg/hr IV of dextrose 50% solution for 5 days to treat hepatic lipidosis and ketosis.

### Regulatory Information

Withdrawal times are not established. However, this drug presents little risk from residues; therefore no withdrawal time is suggested for animals intended for food.

## Diazepam

dye-ay'zeh-pam

**Trade and other names:** Valium and generic brands

**Functional classification:** Anticonvulsant

### Pharmacology and Mechanism of Action

Benzodiazepine. Central acting CNS depressant. Mechanism of action appears to be via potentiation of gamma-aminobutyric acid (GABA)-receptor-mediated effects in CNS because it binds to the GABA binding site. Diazepam is metabolized to desmethyldiazepam (nordiazepam) and oxazepam. These metabolites also have some centrally acting benzodiazepine effects. In dogs, the IV half-life of diazepam is short (<1 hour), but active metabolites are produced. Cats may have decreased capacity for glucuronidation of diazepam and metabolites for clearance and excretion. In cats, the IV half-life is approximately 3.5-5 hours.

### Indications and Clinical Uses

Diazepam is used for sedation, anesthetic adjunct, anticonvulsant, and behavioral disorders. Although it is used as a muscle relaxant, its efficacy for this use is not established. In cats, diazepam has been administered IV for short-term stimulation of appetite. In cats, oral administration has been effective for decreasing urine spraying, but relapses are common when the drug is discontinued. Diazepam is usually administered orally or intravenously. However, it has been shown to be absorbed adequately in dogs from rectal administration and intranasal administration (41% absorption from nasal spray in dogs).

### Precautionary Information

#### Adverse Reactions and Side Effects

Sedation is the most common side effect. In dogs, ataxia and increased appetite can be observed. Diazepam may cause paradoxical excitement and agitation in dogs. In cats, idiopathic fatal hepatic necrosis has been reported. Chronic administration may lead to dependence and a withdrawal syndrome if discontinued. Administration IM or SQ can be painful and irritating. Intravenous injection can cause phlebitis.

#### Contraindications and Precautions

Diazepam is highly dependent on liver blood flow for metabolism. Do not administer to patients with impaired liver function. Long-term use in cats should be avoided because of risk of liver toxicity. Its use for ivermectin-induced CNS intoxication is controversial.

#### Drug Interactions

Diazepam is highly lipophilic and will bind to (adsorb) soft plastic containers, infusion, sets, and fluid bags. Storage of diazepam in such containers is not recommended. Diazepam is not soluble in aqueous solutions. Admixing with aqueous solutions or fluids can result in precipitation.

### Instructions for Use

Clearance in dogs is many times faster than in people (half-life in dogs less than 1 hour), requiring frequent administration. For treatment of status epilepticus,

diazepam solution may be administered intravenously, intranasally, or rectally. Avoid IM administration because of pain from injection and unpredictable absorption.

### Patient Monitoring and Laboratory Tests

Plasma concentrations in the range of 100-250 ng/mL have been cited as the therapeutic range for people. Other references have cited this range as 150 to 300 ng/mL. Although plasma or serum may be analyzed for concentrations of benzodiazepines, there are no readily available tests for monitoring in many veterinary laboratories. Laboratories that analyze human samples may have nonspecific tests for benzodiazepines. With these assays, there may be cross-reactivity among diazepam and the metabolites desmethyldiazepam and oxazepam.

### Formulations

- Diazepam is available in 2-, 5-, and 10-mg tablets and 5-mg/mL solution for injection.

### Stability and Storage

Do not store in soft plastic (polyvinyl chloride [PVC]) containers or fluid bags. Significant adsorption occurs to soft plastic. However, it is compatible with hard plastic, such as syringes. Do not expose to light. Compounded formulations, especially those prepared for transdermal application, may not be stable. Diazepam is practically insoluble in water but is soluble in alcohol and propylene glycol. Diazepam undergoes hydrolysis in water. Diazepam prepared as an oral suspension (1 mg/mL) in various vehicles (pH 4.2) was stable for 60 days.

### Small Animal Dosage

#### Dogs and Cats

- Preanesthetic: 0.5 mg/kg IV.
- Status epilepticus: 0.5 mg/kg IV, 0.5-1 mg/kg sprayed intranasal, or 1 mg/kg rectal; repeat if necessary.
- CRI: 15 mcg/kg/min (1 mg/kg/hr), which can be decreased by 50% in some animals if excessive side effects are observed.
- Appetite stimulant (cats): 0.2 mg/kg IV.
- Behavior treatment (cats): 1-4 mg/cat q12-24h PO.
- Behavior treatment (dogs): 0.5-2 mg/kg q4-6h, PO.

### Large Animal Dosage

#### Cattle, Sheep, and Goats

- 0.02-0.08 mg/kg IV, up to 0.5 mg/kg slowly IV. Dose according to desired effect. Cows may be recumbent after 0.5 mg/kg. Do not administer IM.

#### Horses

- Seizures: 0.1-0.4 mg/kg IV (start with 50-100 mg per horse). CRI for foals: 1-3 mg per hour.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule IV controlled drug

RCI Classification: 2



## Dichlorphenamide

dye-klor-fen'ah-mide

**Trade and other names:** Daranide

**Functional classification:** Diuretic

### Pharmacology and Mechanism of Action

Carbonic anhydrase inhibitor. Diuretic. Dichlorphenamide, like other carbonic anhydrase inhibitors, produces diuresis by inhibiting the reabsorption of bicarbonate in proximal renal tubules via enzyme inhibition. This action results in loss of bicarbonate in the urine and diuresis. The action of carbonic anhydrase inhibitors results in significant urine loss of bicarbonate, alkaline urine, and water.

### Indications and Clinical Uses

Dichlorphenamide is rarely used as a diuretic any longer. More potent and effective diuretic drugs are available, such as the loop diuretics (furosemide). Dichlorphenamide, like other carbonic anhydrase inhibitors, is used primarily to reduce intraocular pressure in animals with glaucoma. Methazolamide is used more often than dichlorphenamide or acetazolamide for this purpose, and other treatment regimens are used more often than carbonic anhydrase inhibitors. Dichlorphenamide, like other carbonic anhydrase inhibitors, is sometimes used to produce a more alkaline urine for management of some urinary calculi.

### Precautionary Information

#### Adverse Reactions and Side Effects

With prolonged use it will deplete bicarbonate if not replenished. Sulfonamide derivative. Some animals sensitive to sulfonamides may be sensitive to dichlorphenamide. Hypokalemia may occur in some patients. Severe metabolic acidosis is rare.

#### Contraindications and Precautions

Use cautiously in animals sensitive to sulfonamides.

#### Drug Interactions

Dichlorphenamide will produce alkaline urine, which may affect clearance of some drugs. Alkaline urine may potentiate the effects of some antibacterial drugs (e.g., macrolides and quinolones).

### Instructions for Use

Dichlorphenamide is not used as a diuretic, but is most commonly used to treat glaucoma or produce alkaline urine. It has been combined with other antiglaucoma agents.

### Patient Monitoring and Laboratory Tests

Monitor ocular pressure for glaucoma treatment. Monitor serum potassium and acid-base status during treatment.

### Formulations

- Dichlorphenamide is no longer commercially available. However, older forms were available in 50-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 3-5 mg/kg q8-12h PO.

## Large Animal Dosage

- No large animal doses are reported.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Dichlorvos

dye'klor-vos

**Trade and other names:** Task, Atgard, DDVP, Verdisol, and Equigard. Also known as dichlorovos.

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Antiparasitic drug. Kills parasites by anticholinesterase action.

## Indications and Clinical Uses

Dichlorvos is used primarily to treat intestinal parasites. Parasites that may be treated include *Toxocara canis* and *Toxascaris leonina* (roundworms), *Ancylostoma caninum*, *Uncinaria stenocephala* (hookworms), and *Trichuris vulpis* (whipworms). However, efficacy against *T. vulpis* may be erratic. In horses, it may be used for the removal and control of bots (*Gastrophilus intestinalis*, *G. nasalis*), large strongyles (*Strongylus vulgaris*, *S. equinus*, *S. edentatus*), small strongyles (of the genera *Cyathostomum*, *Cylicocercus*, *Cylicodontophorus*, *Triodontophorus*, *Poteriostomum*), pinworms (*Oxyuris equi*), and large roundworm (*Parascaris equorum*). In pigs, it is used to treat and control mature, immature, and/or fourth-stage larvae of the whipworm (*Trichuris suis*), nodular worm (*Oesophagostomum* spp.), large roundworm (*Ascaris suum*), and the thick stomach worm (*Ascarops strongylina*).

## Precautionary Information

### Adverse Reactions and Side Effects

Overdoses can cause organophosphate intoxication (treat with pralidoxime chloride and atropine). Signs of toxicity include salivation, diarrhea, difficulty breathing, and muscle twitching.

### Contraindications and Precautions

Do not use in patients with heartworms. Do not administer within 2 days of administration of a cholinesterase-inhibiting drug. Use a split-dosage schedule in animals that are old, heavily parasitized, anemic, or otherwise debilitated. Do not use in young foals, kittens, or puppies less than 2 pounds. Its use may exacerbate clinical signs in animals with respiratory disease, such as bronchitis and obstructive pulmonary disease. Do not allow birds access to feed containing this preparation or to fecal excrement from treated animals.

### Drug Interactions

Do not use with other anticholinesterase drugs. Do not use with other antifilarial agents, muscle relaxants, CNS depressants, or tranquilizers.

## Instructions for Use

Administer in about one third of the regular canned dog food ration or in ground meat. Dogs may be treated with any combination of capsules and/or pellets so that the animal receives a single dose. One half of the single recommended dosage may be given, and the other half may be administered 8 to 24 hours later. For horses, administer in the grain portion of the ration. It may be administered at one half of the single recommended dosage and repeated 8-12 hours later for treatment of old, emaciated, or debilitated subjects or those reluctant to consume medicated feed. Split the dose if heavy parasitism may cause concern over mechanical blockage of the intestinal tract.

## Patient Monitoring and Laboratory Tests

Monitor for parasites as part of a regular parasite control program.

## Formulations

- Dichlorvos is available in 10- and 25-mg tablets. Manufacture of equine formulations has been discontinued.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 26.4-33 mg/kg once PO.

### Cats

- 11 mg/kg once PO.

## Large Animal Dosage

### Pigs

- 11.2-21.6 mg/kg once PO. For pregnant sows, mix into a gestation feed to provide 1000 mg/head daily during last 30 days of gestation, mixed at a rate of 334-500 g/ton of feed. For other pigs, mix at 334 per ton of feed and feed as sole ration for 2 consecutive days (rate of 8.4 pounds of feed per head until the medicated feed has been consumed).

### Horses

- 31-41 mg/kg once PO.

## Regulatory Information

Do not administer to horses intended for food.

For other animals, no regulatory information is available. For extralabel use with-drawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Diclazuril

dih-klaz'yoor-il

**Trade and other names:** Clincox, Protazil pellets for horses.

**Functional classification:** Antiprotozoal

## Pharmacology and Mechanism of Action

Coccidiostat. Diclazuril is a triazinone antiprotozoal that is effective for treating infections caused by *Isospora* spp., *Toxoplasma gondii*, and *Eimeria* spp. and has been used for treating coccidiosis. It also has been used in horses to treat equine protozoal myeloencephalitis (EPM) caused by *Sarcocystis neurona*. Toltrazuril sulfone (ponazuril) is an active metabolite found in serum and cerebrospinal fluid (CSF) of

treated horses. Although the exact mechanism of action is currently under investigation, diclazuril exerts its anti-*S. neurona* effect by inhibiting merozoite production. Pharmacokinetics have been studied in horses. The oral absorption is 1.56% with a half-life of 43-65 hours. Other studies in horses have shown that at a dose of 1 mg/kg and 0.5 mg/kg the half-life is 55, and 87 hours, respectively, with peak concentration of 0.185 and 0.1 mcg/mL, respectively. With repeated dosing to steady-state, the half-life from 0.5 and 1.0 mg/kg was 71 and 54 hours, respectively with peak concentration of 0.97 and 0.9 mcg/mL, respectively. Thus, with chronic dosing the pharmacokinetic profile was similar with 1.0 mg/kg and 0.5 mg/kg to horses.

### Indications and Clinical Uses

Dosage information for diclazuril has been based on approved indications, experimental studies, pharmacokinetic data, and limited clinical experience. Diclazuril has been replaced by ponazuril for treating most cases of EPM in horses.

#### Precautionary Information

##### Adverse Reactions and Side Effects

No specific adverse effects have been reported.

##### Contraindications and Precautions

No contraindications have been reported.

##### Drug Interactions

No drug interactions have been reported.

### Instructions for Use

Administer orally to horses.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. The targeted concentration of diclazuril to inhibit merozoite production of *S. neurona* and *S. falcatula* in bovine turbinate cell cultures is 0.1 ng/ml to achieve >80% inhibition and 1.0 ng/ml to achieve >95% inhibition.

### Formulations

- Diclaruzil pellets for horses is available as 1.56% diclazuril to be mixed as a top-dress on feed for treatment of EPM. One 2-pound bucket treats one horse for 28 days. It is also available as a medicated feed additive for poultry.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

- No dosing information has been reported for small animals.

### Large Animal Dosage

#### Horses

- Treatment of EPM: 1 mg/kg oral as a top-dress on feed for 28 days added to daily ration. It has also been shown that with repeated administration to steady-state, 0.5 mg/kg body weight achieves a similar pharmacokinetic profile as dosing at the FDA labeled dose of 1 mg/kg.
- For prevention of EPM: Top dress feed with pellets: 0.5 mg/kg once every 3 or 4 days.

### Regulatory Information

Do not administer to horses intended for food. Withdrawal time for poultry is 5 days. For other animals, no regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888 USFARAD (1-888-873-2723).

## Dicloxacillin Sodium

dye-kloks-ah-sill'in soe'dee-um

**Trade and other names:** Dynapen and generic

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Dicloxacillin is a beta-lactam antibiotic—a semisynthetic derivative of penicillin. It resembles ampicillin in activity, except it has greater stability against staphylococcal beta-lactamase. Like other antibiotics in this class, it inhibits bacterial cell wall synthesis by binding to penicillin-binding proteins and weakening the cell wall. The spectrum is limited to gram-positive bacteria, especially staphylococci.

### Indications and Clinical Uses

Dicloxacillin has a relatively narrow spectrum of activity. Like cloxacillin and oxacillin, the spectrum of dicloxacillin includes gram-positive bacilli, including beta-lactamase-producing strains of *Staphylococcus*. Therefore it has been used to treat staphylococcal infections in animals, including pyoderma. It is not active against methicillin-resistant *Staphylococcus*. Because of availability of other drugs for small animals to treat this spectrum of bacteria, dicloxacillin is not used commonly. Because it is an oral drug with limited absorption in large animals, its use is limited to small animal oral administration.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects of penicillin drugs are most commonly caused by drug allergy. This can range from acute anaphylaxis when administered, to other signs of allergic reaction when other routes are used. When administered orally (especially with high doses), diarrhea is possible.

#### Contraindications and Precautions

Use cautiously in animals allergic to penicillinlike drugs.

#### Drug Interactions

There are no specific drug interactions. Dicloxacillin is absorbed better on an empty stomach in dogs.

### Instructions for Use

No clinical efficacy studies are available for dogs or cats. In dogs, oral absorption is low and may not be suitable for therapy. Administer on an empty stomach, if possible.

### Patient Monitoring and Laboratory Tests

Use oxacillin as a guide for sensitivity testing. Break points for oxacillin apply to dicloxacillin.

### Formulations

Some formulations have been discontinued. Dicloxacillin has been available in 125-, 250-, and 500-mg capsules and 12.5-mg/mL oral suspension.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with other drugs. Reconstituted oral suspension is stable for 14 days refrigerated. Compounded formulations, especially aqueous formulations, may not be stable.

## Small Animal Dosage

### Dogs and Cats

- 11-55 mg/kg q8h PO.

## Large Animal Dosage

- No dose has been reported for large animals. Oral absorption is low.

## Regulatory Information

No regulatory information is available. Because oral absorption is expected to be minimal, when using systemically in food animals, apply similar withdrawal times as for ampicillin. Alternatively, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Diethylcarbamazine Citrate

dye-eth-il-kar-bam'eh-zeen sih'trate

**Trade and other names:** Caricide, Filaribits, and Nemacide

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Heartworm preventative and anthelmintic. Produces neuromuscular blockade in parasite through inhibition of neurotransmitter that causes paralysis of worms.

## Indications and Clinical Uses

Caricide tablets and some other brands used for heartworm prevention have been voluntarily withdrawn by the sponsor. Because of the availability of other heartworm preventatives, the use of diethylcarbamazine has diminished significantly. Diethylcarbamazine has been used to prevent infection caused by heartworms in dogs. It is administered regularly during heartworm season in endemic areas. It is not effective to treat heartworms once infection is established. Other uses of diethylcarbamazine include control of ascarids infections (*Toxocara canis* and *Toxascaris leonina*) and as an aid in treatment of ascarid infections at higher doses (55-110 mg/kg). In cats, diethylcarbamazine has been used to treat ascarid worm infections (55-110 mg/kg).

## Precautionary Information

### Adverse Reactions and Side Effects

Overdoses cause vomiting. If administered to an animal with positive microfilaria, reactions, including pulmonary reactions, are possible. This drug is a piperazine derivative, which is a class of antiparasitic drugs considered generally safe in animals.

### Contraindications and Precautions

Dogs with established heartworm infections caused by *Dirofilaria immitis* should not receive diethylcarbamazine until they have been treated with an adulticide to kill the adult heartworms, followed by appropriate microfilaricidal treatment. Reactions can occur in animals with positive microfilaria. However, there are no breed sensitivities or other specific contraindications.

### Drug Interactions

No specific drug interactions are reported.

## Instructions for Use

Specific protocols for heartworm administration may be based on the region of country because the time (season) required for heartworm prevention depends on the duration of active mosquitoes during the year. Although diethylcarbamazine is effective to prevent heartworms, it requires almost continual daily treatment for efficacy. Two or three doses should not be missed. Occasionally, some animals vomit immediately after dosing. Administration with food sometimes decreases this reaction. If diethylcarbamazine treatment has been interrupted, the American Heartworm Society recommends switching chemoprophylaxis to macrocyclic lactones (ivermectin and related drugs).

## Patient Monitoring and Laboratory Tests

Monitor heartworm status of patient. It is important to test for microfilaria in animals before prescribing. Manufacturers recommend that animals that are currently receiving diethylcarbamazine be checked for microfilaria every 6 months. Reactions can occur in animals with positive microfilaria.

## Formulations

- Although some brands have been withdrawn by the sponsor, some availability of other diethylcarbamazine tablets may vary with manufacturer and brand name. Not every brand name is available in the sizes listed. Both plain and chewable tablets have been available. Tablet sizes include 30, 45, 50, 60, 100, 120, 150, 180, 200, 300, and 400 mg. Syrup has been available as 60 mg/mL.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- Heartworm prophylaxis: 6.6 mg/kg q24h PO.
- Treatment of ascarids: 55-110 mg/kg PO, as a single treatment (110 mg/kg dose may be divided into twice per day).

### Cats

- Ascarid treatment: 55-110 mg/kg PO. When treating ascarid parasites, consider repeating treatment in 10-20 days to remove immature worms.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available.

For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Diethylstilbestrol

dye-eth-il-stil-bess'trole

**Trade and other names:** DES and generic brands

**Functional classification:** Hormone

## Pharmacology and Mechanism of Action

Diethylstilbestrol, known as DES, is a synthetic drug with estrogen effects. It differs from steroid compounds because it does not have a steroid ring. It is used for estrogen replacement in animals. When used to treat urinary incontinence, the action of DES is believed to increase sensitivity of alpha receptors in the urinary sphincter to restore continence.

## Indications and Clinical Uses

DES is most commonly used to treat estrogen-responsive incontinence in dogs. Phenylpropanolamine (PPA) has been used in dogs when DES therapy is no longer effective. DES also has been used to induce abortion in dogs. Commercial forms of DES are no longer available, but it is available through some compounding pharmacies. Conjugated estrogens (e.g., Premarin at 20 mcg/kg twice weekly) have been used in some dogs when DES or other estrogens have been unavailable. There is now an approved form of estriol for dogs (Incurin) that can be used instead of DES for treatment of incontinence in female dogs (*see section on estriol for more details*).

### Precautionary Information

#### Adverse Reactions and Side Effects

Side effects that are caused by excess estrogen may occur. Estrogen therapy may increase risk of pyometra and estrogen-sensitive tumors. Although bone marrow depression (particularly anemia) has been reported from administration of other estrogens in dogs and has been cited as a potential risk, it is a rare complication of DES therapy.

#### Contraindications and Precautions

DES has been associated with development of cancer, and human exposure should be minimized as much as possible (the use is prohibited in food animals). Although not reported as a significant clinical problem with DES, problems with anemia have occurred with administration of high doses of estrogens to animals.

#### Drug Interactions

No significant drug interactions have been reported for animals. However, in people, administration of estrogens increases thyroid-binding globulin and may decrease the active form of thyroid hormone ( $T_4$ ) in patients receiving thyroid supplementation.

## Instructions for Use

Doses listed are for treating urinary incontinence and vary depending on response. Titrate dose to individual patient's response. Although used to induce abortion, it was not efficacious in one study that administered 75 mcg/kg.

## Patient Monitoring and Laboratory Tests

Monitor CBC to detect signs of bone marrow toxicity. Monitor  $T_4$  levels if patients are hypothyroid and receiving supplementation.

## Formulations

- DES has been available in 1- and 5-mg tablets and 50-mg/mL injection. DES is no longer marketed commercially in the US, but it is available from compounding pharmacies.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been reported. However, compounded



## 238 Difloxacin Hydrochloride

tablets are available from compounding pharmacies, and anecdotal information indicates that they are effective.

### Small Animal Dosage

#### Dogs

- Dose ranges from 0.1 to 1 mg per dog, q24h PO. Size of dose is proportional to size of dog. Continue daily dose for 5 days, then reduce frequency of administration to two or three times per week.

#### Cats

- 0.05-0.1 mg/cat q24h PO.

### Large Animal Dosage

- No dose is available for large animals. Use in animals intended for food is prohibited.

### Regulatory Information

Administering DES to animals that produce food is prohibited.

## Difloxacin Hydrochloride

dye-floks'ah-sin hye-droe-klor'ide

**Trade and other names:** Dicural

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Fluoroquinolone antibacterial drug. Acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. Bactericidal with broad spectrum of activity. Antibacterial activity includes *Escherichia coli*, *Klebsiella* spp., *Pasteurella* spp., and other gram-negative bacilli. Activity against *Pseudomonas aeruginosa* is less than for other gram-negative bacilli. Activity against gram-positive cocci includes *Staphylococcus*, *Streptococcus* and *Enterococcus* are more resistant. In horses, it has an oral half-life of 10.8 hours and bioavailability of 68%.

### Indications and Clinical Uses

Difloxacin, like other fluoroquinolones, is used for a variety of infections, including skin infections, wound infections, and pneumonia. Unlike other fluoroquinolones, difloxacin does not have high renal clearance. Urine concentrations may not be sufficient for some UTIs.

### Precautionary Information

#### Adverse Reactions and Side Effects

High concentrations may cause CNS toxicity, especially in animals with renal failure. Difloxacin may cause some nausea, vomiting, and diarrhea at high doses. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4 weeks to 28 weeks of age. Large, rapidly growing dogs are the most susceptible. Safety in cats has not been reported. It has not been reported if there is a potential to cause retinal ocular injury in cats.

#### Contraindications and Precautions

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures, such as epileptics. Avoid use in cats unless safety has been established.

### Drug Interactions

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, or calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

### Instructions for Use

Dose range can be used to adjust dose depending on severity of infection and susceptibility of bacteria. Bacteria with low MIC values can be treated with a low dose; susceptible bacteria with higher MIC values should be treated with a higher dose. Difloxacin is primarily eliminated in feces rather than urine (urine is less than 5% of clearance). Sarafloxacin is an active desmethyl metabolite but produced in low amounts. Oral absorption in horses is low and should only be used for bacteria with MIC less than 0.12 mcg/mL.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 0.5$  mcg/mL for canine pathogens. Other fluoroquinolones may be used in some cases to estimate susceptibility to this fluoroquinolone. However, if ciprofloxacin is used to test susceptibility to *P. aeruginosa*, ciprofloxacin may be several times more active than other fluoroquinolones.

### Formulations

- Difloxacin is available in 11.4-, 45.4-, and 136-mg tablets. (In some countries, 5% injectable is available.)

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated, but has been mixed with simple syrup (100 mg/mL) for horses.

### Small Animal Dosage

#### Dogs

- 5-10 mg/kg q24h PO.

#### Cats

- No dosing information for cats is available. There is no safety information available.

### Large Animal Dosage

- Horses: 5 mg/kg PO, q24h.

### Regulatory Information

Do not administer to animals intended for food.

## Digitoxin

dih-jih-toks'in

**Trade and other names:** Digimerck (European)

**Functional classification:** Cardiac inotropic agent

## **Pharmacology and Mechanism of Action**

Cardiac inotropic agent. Digitoxin increases cardiac contractility and decreases heart rate. The mechanism is via inactivation of cardiac muscle sodium–potassium ATPase and increased intracellular accumulation of calcium, triggering calcium release from the sarcoplasmic reticulum. In addition, neuroendocrine effects include sensitization of baroreceptors, which decreases heart rate. Beneficial effects for heart failure may be via these neuroendocrine effects.

## **Indications and Clinical Uses**

Digitoxin is indicated in patients with myocardial failure and to control the rate of supraventricular tachycardias. Digitoxin formulation availability for treating patients is limited. Digitoxin is no longer obtained in the US. Subsequently, most of the digitoxin use has been replaced by digoxin. Digoxin is an active metabolite of digitoxin and may be used instead of digitoxin.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Digitalis glycosides have narrow therapeutic index. Digitoxin may cause a variety of arrhythmias in patients (e.g., AV block and ventricular tachycardia). It frequently causes vomiting, anorexia, and diarrhea. Digitoxin has adverse effects potentiated by hypokalemia, reduced by hyperkalemia.

#### **Contraindications and Precautions**

Do not administer to animals with AV block or at risk for other serious arrhythmias. Do not administer to animals with potassium electrolyte abnormalities.

#### **Drug Interactions**

High potassium will diminish clinical effect; low potassium will enhance effect and toxicity. Quinidine may increase plasma concentrations. Calcium-channel blocking drugs and beta blockers may potentiate action on AV node conduction.

## **Instructions for Use**

Use of digitoxin has diminished in recent years in favor of digoxin. If available, it may be used with other cardiac drugs.

## **Patient Monitoring and Laboratory Tests**

Monitor serum digoxin concentrations in patients to determine optimum therapy. When monitoring, collect blood samples 2-6 hours after dosing. The therapeutic range is 10-30 ng/mL.

## **Formulations**

- Digitoxin was once available in 0.05- and 0.1-mg tablets. (It is no longer available and must be obtained from European sources.)

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## **Small Animal Dosage**

### **Dogs**

- 0.02-0.03 mg/kg q8h PO.

## **Large Animal Dosage**

### **Cattle**

- 50-60 mcg/kg q6h IV.

## Regulatory Information

Do not administer to cattle intended for food.

RCI Classification: 4

## Digoxin

dih-joks'in

**Trade and other names:** Lanoxin and Cardoxin

**Functional classification:** Cardiac inotropic agent

## Pharmacology and Mechanism of Action

Cardiac inotropic agent. Digoxin increases cardiac contractility and decreases heart rate. The mechanism is via inactivation of cardiac muscle sodium–potassium ATPase and increased intracellular availability of calcium, triggering calcium release from sarcoplasmic reticulum. In addition, neuroendocrine effects include sensitization of baroreceptors, which decreases heart rate by increasing vagal tone. Beneficial cardiac effects may be caused by decreased heart rate and suppression of the AV node to inhibit reentrant cardiac arrhythmias via these neuroendocrine effects.

## Indications and Clinical Uses

Digoxin is used in heart failure for inotropic effect and decreased heart rate in dogs, cats, and occasionally other animals. It is used in supraventricular arrhythmias to decrease ventricular response to atrial stimulation via suppression of the AV node. Digoxin may be used with other drugs for heart failure such as ACE inhibitors (e.g., enalapril), diuretics (furosemide), and vasodilators.

## Precautionary Information

### Adverse Reactions and Side Effects

Digitalis glycosides such as digoxin have a narrow therapeutic index. They may cause a variety of arrhythmias in patients (e.g., AV and ventricular tachycardia) and may produce delayed after depolarization-induced arrhythmias. Digoxin frequently causes vomiting, anorexia, and diarrhea. Digoxin adverse effects are potentiated by hypokalemia and reduced by hyperkalemia.

### Contraindications and Precautions

Some breeds of dogs (Doberman pinscher) and cats are more sensitive to adverse effects.

### Drug Interactions

High potassium will diminish clinical effect; low potassium will enhance effect and toxicity. Digoxin is a substrate for cytochrome P-450 enzymes and p-glycoprotein, and many drugs are capable of increasing digoxin concentrations, including quinidine, aspirin, clarithromycin (and other macrolides), and chloramphenicol (see Appendixes I and J for list of inhibitors). Administration of phenobarbital chronically may decrease digoxin concentrations by increasing clearance. Calcium-channel blockers and beta blockers will potentiate action on AV node conduction, increasing the risk of AV block. Digoxin is absorbed better in an acid stomach, and proton pump inhibitors or H<sub>2</sub> blockers may reduce oral absorption.

## Instructions for Use

When dosing, calculate dose on lean body weight. Doses should be 10% less for elixir because of increased absorption. When used to treat atrial fibrillation in dogs, combined with diltiazem, it may produce greater reduction in ventricular rate than either drug alone.

## Patient Monitoring and Laboratory Tests

Monitor patients carefully. Monitor serum digoxin concentrations in patients to determine optimum therapy. Therapeutic range is 0.8-1.5 ng/mL 8-10 hours after a dose. Some cardiologists recommend concentrations of 0.9-1.0 ng/mL and below for treating heart failure and to reduce heart rate to 140-160 bpm. Adverse effects are common at concentrations above 3.5 ng/mL, but in some sensitive patients, this may be as low as 2.5 ng/mL. Patients may be monitored with ECG to detect digoxin-induced arrhythmias.

## Formulations

- Digoxin is available in 0.0625-, 0.125-, and 0.25-mg tablets and 0.05- and 0.15- mg/mL elixir.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is not stable if mixed with low-pH solutions (pH <3). Do not compound oral tablets with other medications.

## Small Animal Dosage

### Dogs

- 0.005-0.011 mg/kg q12h PO (dose used by most cardiologists).
- Alternatively, doses have varied based on dog's body weight: dogs < 20 kg: 0.005-0.01 mg/kg q12h and if >20 kg: 0.22 mg/m<sup>2</sup> q12h PO (subtract 10% for elixir).
- Rapid digitalization: 0.0055-0.011 mg/kg q1h IV to effect.
- Atrial fibrillation: 0.005 mg/kg q12h PO (may be combined with diltiazem at 3 mg/kg q12h PO).

### Cats

- 0.008-0.01 mg/kg q48h PO. (Approximately one fourth of a 0.125-mg tablet/cat).

## Large Animal Dosage

### Cattle

- 22 mcg/kg (0.022 mg/kg) IV loading dose, followed by 0.86 mcg/kg/hr IV or multiple doses of 3.4 mcg/kg q4h. Plasma concentrations to monitor are similar as for other animals.

### Horses

- 2 mcg/kg (0.002 mg/kg) IV q12h.
- 15 mcg/kg (0.015 mg/kg) q12h PO.

## Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 4

## Dihydratichysterol

dye-hye-droe-tak-iss'ter-ole

**Trade and other names:**

**Functional classification:** Vitamin

**D**

### Pharmacology and Mechanism of Action

Vitamin D analogue. Vitamin D promotes absorption and utilization of calcium.

### Indications and Clinical Uses

Dihydratichysterol is used as treatment of hypocalcemia, especially hypoparathyroidism associated with thyroidectomy. The most common use is for replacement in cats that have had thyroidectomy for treatment of hyperthyroidism. Calcitriol is another drug that is used to regulate calcium concentrations in animals (see Calcitriol).

### Precautionary Information

#### Adverse Reactions and Side Effects

Overdose may cause hypercalcemia.

#### Contraindications and Precautions

Avoid use in pregnant animals because it may cause fetal abnormalities.

#### Drug Interactions

No specific drug interactions are reported for animals. However, use cautiously with high doses of preparations containing calcium. Use with caution with thiazide diuretics.

### Instructions for Use

Doses for individual patients should be adjusted by monitoring serum calcium concentrations.

### Patient Monitoring and Laboratory Tests

Monitor serum calcium concentration.

### Formulations

- No formulations are currently available in the US. It can only be obtained from some compounding pharmacies. Older formulations consisted of 0.125-mg capsules; 0.5-mg/mL oral liquid (20% alcohol); and 125-, 200-, and 400-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dog and Cats

- 0.01 mg/kg/day PO.
- Acute treatment: 0.02 mg/kg initially, then 0.01-0.02 mg/kg q24-48h PO thereafter. The dose should be adjusted on the basis of measuring calcium concentrations. Effective doses can range as high as 0.1 to 0.3 mg/kg.

### Large Animal Dosage

- No large animal doses are reported.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Diltiazem Hydrochloride**

dil-tye'ah-zem hye-droe-klor'ide

**Trade and other names:** Cardizem and Dilacor

**Functional classification:** Calcium-channel blocker

**Pharmacology and Mechanism of Action**

Calcium-channel blocking drug. Diltiazem blocks calcium entry into cells via blockade of voltage-dependent slow calcium channel. Via this action, it produces vasodilation, negative chronotropic effects, and negative inotropic effects. However, the action on cardiac tissue (SA node and AV node) predominates over other effects. Half-life in dogs is approximately 3 hours (range 2.5-4 hrs), and it is shorter in horses (1.5 hrs).

**Indications and Clinical Uses**

Diltiazem is used primarily for control of supraventricular arrhythmias, systemic hypertension, and hypertrophic cardiomyopathy. It also is used for atrial flutter, AV nodal reentry arrhythmias, and other forms of tachycardia. Diltiazem is more effective on heart tissues (AV node and SA node) than on blood vessels. It should not be used as a primary treatment of hypertension and to produce vasodilation; one of the dihydropyridines calcium-channel blocking drugs (e.g., amlodipine) is preferred. In cats, it is considered one of the drugs of choice for treatment of feline hypertrophic cardiomyopathy (HCM). In dogs, diltiazem has been used to treat acute renal failure. It may improve renal perfusion by decreasing renal vasoconstriction and improving renal perfusion. In horses, diltiazem may be effective for atrial fibrillation. However, treated horses had variable results, and some developed hypotension and sinus arrest. Transdermal administration of diltiazem has not been shown to be effective in cats.

**Precautionary Information****Adverse Reactions and Side Effects**

Hypotension, myocardial depression, bradycardia, and AV block are the most important adverse effects. If acute hypotension occurs, treat with aggressive fluid therapy and administration of calcium gluconate or calcium chloride. It may cause anorexia in some patients. High doses in cats have caused vomiting. When cats were administered 60 mg of Dilacor XR, it produced lethargy, GI disturbances, and weight loss in 36% of cats.

**Contraindications and Precautions**

Do not inject rapidly when administering IV. Do not administer to patients with hypotension.

**Drug Interactions**

Calcium-channel blocking drugs have been associated with drug interactions in people by interfering with drug metabolism. These interactions have not been documented in veterinary patients but are possible because of similar mechanisms. Therefore use with caution when administering other drugs that may be p-glycoprotein (efflux protein produced by multidrug resistance [MDR] gene) substrates. (See Appendixes J and K.) Do not mix IV solutions with furosemide.

## Instructions for Use

Diltiazem is preferred over verapamil in patients with heart failure because of less myocardial depression. When used to treat atrial fibrillation in dogs, combined with digoxin, it may produce greater reduction in ventricular rate than either drug alone. See detailed instructions for cats in “[Small Animal Dosage](#)” section.

## Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during treatment. Monitor blood pressure with acute treatment for atrial fibrillation. If blood concentrations are monitored, to produce a reduction in heart rate, 80-290 ng/mL are necessary in people and 60-120 ng/mL in dogs.

## Formulations

- Diltiazem is available in 30-, 60-, 90-, and 120-mg tablets; 60-, 90-, 120-, 180-, 240-, and 300-mg extended release capsules; and in a 5-mg/mL injection solution.
- Dilacor XR has three or four tablets in one unit. The capsule may be opened to release the individual tablets for oral dosing in dogs and cats.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Extended-release tablets are difficult to manipulate for pet owners. Compounded transdermal formulations may not be stable. Compounded oral formulations, prepared with various sugars and flavorings, were stable for 50-60 days. Injectable solution may be mixed with IV fluids but should be discarded after 24 hours. Do not freeze.

## Small Animal Dosage

### Dogs

- For most uses: 0.5-1.5 mg/kg q8h PO. For atrial fibrillation, doses as high as 5 mg/kg q12h PO have been used as monotherapy, or a combination of diltiazem (3 mg/kg q12h PO) plus digoxin (0.005 mg/kg q12h, PO) has been used.
- Atrial fibrillation: 0.05-0.25 mg/kg IV administered q5min to effect.
- Supraventricular tachycardia: 0.25 mg/kg over 2 min IV (repeat if necessary). First, inject 0.25 mg/kg, then wait 20 minutes for response before repeating. CRI: 0.15-0.25 mg/kg IV over 2 minutes, then 1-8 mcg/kg/min.
- Acute renal failure: 0.2 mg/kg IV (slowly), followed by 3-5 mcg/kg/min CRI.

### Cats

- 1.75-2.4 mg/kg q8h PO. Most common dose in cats with immediate-release formulations is 7.5-10 mg per cat q8h PO, with frequency reduced to q12h in some cats.
- Dilacor XR or Cardizem CD: 10 mg/kg once daily PO. Extended-release tablets can be more difficult to use in cats compared to other tablets, but have been used at 30 or 60 mg per cat (see later).
- Tablets are difficult to break for use in cats. Note that “XR,” “SR,” and “CD” all refer to slow-release formulations. Dilacor XR-240 mg contains four 60-mg tablets. XR-180 contains three 60-mg tablets. Slow- and extended-release tablets are not recommended for routine use in cats because they produce inconsistent plasma concentrations that may result in ineffective treatment in some and adverse effects in others. Based on available information for cats, use either Dilacor XR 30 or Dilacor XR 60. The dose of 30 mg per cat of Dilacor XR (extended-release tablets) produced fewer adverse effects than 60 mg per cat.



## Large Animal Dosage

### Horses

- 0.125 mg/kg IV over at least 2 minutes. Repeat every 10 minutes as needed, or until total dose of 1.1 mg/kg. Doses as high as 1-2 mg/kg have been used in research animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Dimenhydrinate

dye-men-hye drih-nate

**Trade and other names:** Dramamine (Gravol in Canada)

**Functional classification:** Antihistamine

## Pharmacology and Mechanism of Action

Antihistamine ( $H_1$ -blocker). Diphenhydramine is the active moiety of dimenhydrinate.

Similar to other antihistamines, it acts by blocking the  $H_1$  receptor and suppresses inflammatory reactions caused by histamine. The  $H_1$  blockers have been used to control pruritus and skin inflammation in dogs and cats; however, success rates in dogs have not been high. Commonly used antihistamines include clemastine, chlorpheniramine, diphenhydramine, and hydroxyzine. Dimenhydrinate is converted to active diphenhydramine. Dimenhydrinate also has central-acting antiemetic properties, possibly by acting on the vomiting center or via the chemoreceptor-trigger zone (CRTZ).

## Indications and Clinical Uses

Dimenhydrinate is used to prevent allergic reactions and for pruritus therapy in dogs and cats. However, success rates for treatment of pruritus have not been high. In addition to the antihistamine effect for treating allergies, dimenhydrinate, like other antihistamines, acts as an antiemetic via the drug effects on the centers that control vomiting in animals. Antihistamines used as antiemetics are administered for motion sickness, vomiting induced by chemotherapy, and GI disease that stimulates vomiting.

## Precautionary Information

### Adverse Reactions and Side Effects

Sedation is the most common side effect. Sedation is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to the block of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors. Antimuscarinic effects (atropinelike effects) also are common, including dry mouth and decreased GI secretions.

### Contraindications and Precautions

Antimuscarinic effects (atropinelike effects) are common. Do not use in conditions for which anticholinergic drugs may be contraindicated, such as glaucoma, ileus, or cardiac arrhythmias.

### Drug Interactions

No drug interactions are reported. However, use with other sedatives and tranquilizers may increase sedation.

## Instructions for Use

Like other antihistamines, there have been no clinical studies on the use of dimenhydrinate. It is primarily used empirically for treatment of vomiting and to prevent allergic reactions.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Dimenhydrinate is available in 50-mg tablets and 50-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 4-8 mg/kg q8h PO, IM, or IV.

### Cats

- 12.5 mg/cat q8h IV, IM, or PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Dimercaprol

dye-mer-cap'role

**Trade and other names:** British anti-lewisite (BAL) in oil

**Functional classification:** Antidote

## Pharmacology and Mechanism of Action

Chelating agent. Dimercaprol is also known as BAL. It is a dithiol chelating agent for chelating with heavy metals. It binds to arsenic, lead, and mercury to treat toxicosis.

## Indications and Clinical Uses

Used to treat lead, gold, mercury, and arsenic toxicity. There are two formulations: dimercaptopropane-1-sulfonic acid (DMPS) and meso-2,3-dimercaptosuccinic acid. Because these are not readily available, they may be compounded from a bulk source.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are not reported in veterinary medicine. In people, sterile abscesses occur at the injection site. High doses have caused seizures, drowsiness, and vomiting.

### Contraindications and Precautions

Dimercaprol is used only to treat intoxications.

### Drug Interactions

There are no drug interactions reported.

**Instructions for Use**

Use as soon as possible after intoxicant exposure. Alkalinization of urine will increase toxin removal. For lead intoxication, dimercaprol may be used with edetate calcium.

**Patient Monitoring and Laboratory Tests**

Heavy metal concentrations can be measured to assess treatment.

**Formulations**

- Dimercaprol is available in an injection that must be prepared by compounding.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage**

- 4 mg/kg q4h IM.

**Large Animal Dosage**

- 4 mg/kg q4h IM.

**Regulatory Information**

Withdrawal time: 5 days for milk and meat (extralabel use).

**Dimethyl Sulfoxide (DMSO)**

di-meth-il sulf-ok-sīde

**Trade and other names:** DMSO and Domoso

**Functional classification:** Anti-inflammatory

**Pharmacology and Mechanism of Action**

DMSO is a solvent that is a byproduct of the paper-making process. It is highly hygroscopic (water absorbing). It readily displaces water and will penetrate cell membranes, skin, and mucosa easily. It produces anti-inflammatory, antifungal, and antibacterial properties. The clinical anti-inflammatory action of DMSO is uncertain. It may produce anti-inflammatory or protective effects on cell membranes via its ability to scavenge oxygen-derived free radicals. In horses, at a dose of 1 g/kg, the half-life is 8.6 hours. Twenty-six percent of the administered dose was excreted in the urine. In dogs, the half-life is 36 hours.

**Indications and Clinical Uses**

DMSO is administered topically and systemically (IV) for treatment of various inflammatory conditions. It is popular in horses for treatment of laminitis, arthritis, pneumonia, intestinal ischemia, synovitis, and nervous system injuries. Despite popular use, there are no published reports of efficacy for clinical use, and evidence to support use as an anti-inflammatory agent in treatment of clinical disease is primarily anecdotal. There is no evidence to support use to protect ischemic reperfusion injury in the equine intestine, to treat laminitis, or to improve neurologic disease. It does not promote drug penetration across the blood-brain barrier.

## Precautionary Information

### Adverse Reactions and Side Effects

DMSO is irritating to skin and mucosal membranes. It is hygroscopic and induces release of histamine in skin. Long-term use has produced ocular lens changes in laboratory animals. Concentrated DMSO, when administered IV, will cause significant hemolysis. Intravenous use also has been associated with hemoglobinemia, acute colic, diarrhea, myositis, muscle tremors, and collapse. These reactions are more likely at doses of 2 g/kg or greater. DMSO produces a strong odor when administered.

### Contraindications and Precautions

Although many veterinarians administer it systemically, DMSO is not approved for this use. It may enhance transdermal absorption of toxicants and contaminants on the skin. Do not administer IV at concentrations >10% or at doses >1 g/kg. Do not administer concentrated solution systemically.

### Drug Interactions

DMSO is a strong solvent. It will dissolve other compounds. It may act as a penetration enhancer and increase transmembrane penetration of other compounds.

## Instructions for Use

Dilute prior to use to 10% for IV infusion. Doses vary widely among veterinarians. Dose listed of 1 g/kg is common, but ranges of 0.2-4 g/kg have been cited in the literature for horses.

## Patient Monitoring and Laboratory Tests

Monitor CBC during use.

## Formulations

- DMSO is available in a solution.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with other compounds, unless it is done immediately prior to administration.

## Small Animal Dosage

### Dogs and Cats

- 1 g/kg IV slowly. Do not administer solutions stronger than 10%.

## Large Animal Dosage

### Horses and Cattle

- 1 g/kg IV slowly. Dilute prior to use. Do not administer concentrations >10%. For most conditions, administration is every 12 hours.

## Regulatory Information

Not approved for use in animals intended for food. No withdrawal times are available.

RCI Classification: 5

## Dinoprost Tromethamine

dye'noe-prahst troe-meth'ah-meen

**Trade and other names:** Lutalyse, Prostin F2 alpha, ProstaMate, Prostaglandin F2 alpha, and PGF2 alpha

**Functional classification:** Prostaglandin

### Pharmacology and Mechanism of Action

Dinoprost is a prostaglandin (PGF<sub>2</sub> alpha) that induces luteolysis. Prostaglandin F<sub>2</sub> and its analogues have a direct luteolytic action on the corpus luteum. After injection, it will produce a functional regression of the corpus luteum (luteolysis). In non-pregnant cycling cattle, this effect will result in starting estrus 2 to 5 days after injection. In pregnant animals, it will terminate pregnancy. In animals with prolonged luteal activity that have pyometra, mummified fetus, or luteal cysts, the luteolysis usually results in resolution of the problem and return to normal cycling.

### Indications and Clinical Uses

Dinoprost is used for estrus synchronization in cattle and horses by causing luteolysis. In horses and cattle, it is used to control timing of estrus in estrus-cycling females and in clinically anestrus females that have a corpus luteum. In pigs, dinoprost is used to induce parturition when given within 3 days of farrowing. In dogs, dinoprost has been used to treat open pyometra. In cattle, dinoprost has been used for treatment of chronic endometritis.

In large animals, dinoprost is used to induce abortion in the first 100 days of gestation, but use for inducing abortion in small animals has been questioned.

### Precautionary Information

#### Adverse Reactions and Side Effects

Prostaglandin F<sub>2</sub> alpha causes increased smooth muscle tone, resulting in diarrhea, abdominal discomfort, bronchoconstriction, and increase in blood pressure. In small animals, other side effects include vomiting. Induction of abortion may cause retained placenta.

#### Contraindications and Precautions

Do not administer intravenously. Dinoprost induces abortion in pregnant animals. Use caution when handling this drug by veterinarians, animal owners, and technical help. It should not be handled by pregnant women. Absorption through intact human skin is possible. People with respiratory problems also should not handle dinoprost.

#### Drug Interactions

According to the label, dinoprost should not be used with NSAIDs because these drugs inhibit synthesis of prostaglandins. However, NSAIDs should not affect concentrations of PGF<sub>2</sub> alpha administered by this product. When using oxytocin concurrently, it should be used cautiously because there is a risk of uterine rupture.

### Instructions for Use

Use in treating pyometra should be monitored carefully. If pyometra is not open, severe consequences may result. When used in cattle, after a single injection, cattle should be bred at the usual time relative to estrus. When administering two injections, cattle can be bred after the second injection, either at the usual time relative to

detected estrus or at about 80 hours after the second injection. Estrus is expected to occur 1 to 5 days after injection if a corpus luteum was present. Cattle that do not become pregnant will be expected to return to estrus in about 18-24 days. When used in cattle to induce abortion, it should be used only during the first 100 days of gestation. Cattle that abort will do so within 35 days after injection.

In pigs, administer within 3 days of predicted farrowing for parturition induction. Farrowing should start in approximately 30 hours.

### Patient Monitoring and Laboratory Tests

When used for estrus synchronization, monitor for signs of estrus. Animals should be bred at usual time relative to estrus.

### Formulations

- Dinoprost is available in a 5-mg/mL solution for IM injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- Pyometra: 0.1-0.2 mg/kg, once daily for 5 days SQ.
- Terminate pregnancy: 0.025-0.05 mg (25-50 mcg)/kg q12h IM.

#### Cats

- Pyometra: 0.1-0.25 mg/kg, once daily for 5 days SQ.
- Terminate pregnancy: 0.5-1 mg/kg IM for 2 injections.

### Large Animal Dosage

#### Cattle

- Terminate pregnancy: 25-mg total dose, administered once IM.
- Estrus synchronization: 25 mg (5 mL) IM once or twice at 10-12-day intervals.
- Pyometra: 25 mg administered once IM.

#### Horses

- Estrus synchronization: 1 mg/100 pounds (1 mg/45 kg) or 1-2 mL administered once IM. Mares should return to estrus within 2-4 days and ovulate 8-12 days after treatment.

#### Pigs

- Induction of parturition: 10 mg (2 mL) administered once IM. Parturition occurs within 30 hours.

### Regulatory Information

Do not administer to horses intended for food.

To be used in beef cattle and nonlactating dairy cows only.

## Diphenhydramine Hydrochloride

dye-fen-hye'drah-meen hye-droe-klor'ide

**Trade and other names:** Benadryl

**Functional classification:** Antihistamine

## Pharmacology and Mechanism of Action

Antihistamine ( $H_1$  blocker). Diphenhydramine is the active moiety of dimenhydrinate (Dramamine). Similar to other antihistamines, it acts by blocking the  $H_1$  receptor ( $H_1$ ) and suppresses inflammatory reactions caused by histamine. Commonly used antihistamines include clemastine, chlorpheniramine, diphenhydramine, and hydroxyzine.

## Indications and Clinical Uses

Diphenhydramine, like other antihistamines, is used to prevent allergic reactions and for pruritus therapy in dogs and cats. However, success rates for treatment of pruritus have not been high. In addition to the antihistamine effect for treating allergies, these drugs block the effect of histamine in the vomiting center, vestibular center, and other centers that control vomiting in animals.

## Precautionary Information

### Adverse Reactions and Side Effects

Sedation is the most common side effect. Sedation is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to block of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors. Antimuscarinic effects (atropinelike effects) also are common, including dry mouth and decreased GI secretions. Excitement has been observed in cats and other animals at high doses.

### Contraindications and Precautions

Antimuscarinic effects (atropinelike effects) are common. Do not use in conditions for which anticholinergic drugs may be contraindicated, such as glaucoma, ileus, or cardiac arrhythmias.

### Drug Interactions

There are no specific drug interactions. However because of anticholinergic (atropinelike) effects, it may counteract drugs that are administered for a parasympathomimetic action (e.g., drugs used to stimulate intestinal motility).

## Instructions for Use

Antihistamine used primarily for allergic disease in animals. These drugs also can be used to treat or prevent vomiting in animals. Clinical studies documenting efficacy have been limited. Most use is empirical with doses extrapolated from human use.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Diphenhydramine is available OTC in a 2.5-mg/mL elixir, 25- and 50-mg capsules and tablets, and 50-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Protect from freezing.

## Small Animal Dosage

### Dogs

- 2.2 mg/kg q8-12h PO, IM, or SQ.  
For large dogs, this is equivalent to an oral dose of 25 or 50 mg per dog.

### Cats

- 2-4 mg/kg q6-8h PO.
- 1 mg/kg q8h IV or IM.

## Large Animal Dosage

- 0.5-1 mg/kg as a single dose, as needed, IM.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Diphenoxylate

dye-fen-oks'ih-late

**Trade and other names:** Lomotil

**Functional classification:** Antidiarrheal

## Pharmacology and Mechanism of Action

Opiate agonist. Binds to mu-opiate receptors in intestine and stimulates smooth muscle segmentation in intestine, decreases peristalsis, and enhances fluid and electrolyte absorption.

## Indications and Clinical Uses

Diphenoxylate is used for acute treatment of nonspecific diarrhea. It has primarily a local effect. Loperamide (Imodium) has a similar action and has become more popular for this indication. An additional use, not often used in veterinary medicine, is as an antitussive.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects have not been reported in veterinary medicine. Diphenoxylate is poorly absorbed systemically and produces few systemic side effects. Excessive use can cause constipation.

### Contraindications and Precautions

Do not use in patients with diarrhea caused by infectious causes. Opiates should not be used for chronic treatment of diarrhea.

### Drug Interactions

There are no specific drug interactions reported. However, use cautiously with other opiates and other drugs that may cause constipation (e.g., antimuscarinic drugs).

## Instructions for Use

Doses are based primarily on empiricism or extrapolation of human dose. Clinical studies have not been performed in animals. Diphenoxylate contains atropine, but the dose is not high enough for significant systemic effects.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Diphenoxylate is available in 2.5-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.



## 254 Dipyridamole

### Small Animal Dosage

#### Dogs

- 0.1-0.2 mg/kg q8-12h PO. Antitussive doses have been as high as 0.5 mg/kg q12h PO.

#### Cats

- 0.05-0.1 mg/kg q12h PO.

### Large Animal Dosage

- No use in large animals is reported.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). Schedule V controlled drug.

RCI Classification: 4

## Dipyridamole

dye-peer-id'ah-mole

**Trade and other names:** Persantine

**Functional classification:** Anticoagulant

### Pharmacology and Mechanism of Action

Platelet inhibitor. Mechanism of action is attributed to increased levels of cyclic adenosine monophosphate (cAMP) in platelet, which decreases platelet activation.

### Indications and Clinical Uses

In people, dipyridamole has been used to prevent thromboembolism and hypercoagulable states. However, use of dipyridamole has been infrequent in animals. It may be indicated in clinical conditions in which platelet inhibition is desired. It is indicated primarily to prevent thromboembolism. It is more common to administer other platelet inhibitors such as clopidogrel, with and without aspirin.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. However, bleeding problems are expected in animals prone to coagulopathies or receiving other anticoagulants.

#### Contraindications and Precautions

Do not use in animals with bleeding problems.

#### Drug Interactions

Aspirin may potentiate effects.

### Instructions for Use

Dipyridamole is used primarily in people to prevent thromboembolism. Use in animals has not been reported. When used in people, it is combined with other antithrombotic agents (e.g., warfarin).

### Patient Monitoring and Laboratory Tests

It may be necessary to monitor bleeding times in some animals.

## Formulations

- Dipyridamole is available in 25-, 50-, and 75-mg tablets and 5-mg/mL injection. It is also available combined with aspirin as 200 mg dipyridamole plus 25 mg aspirin (Aggrenox).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Compounded oral formulations have been stable for 60 days.

## Small Animal Dosage

### Dogs and Cats

- 4-10 mg/kg q24h PO.

## Large Animal Dosage

- No use in large animals is reported.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Dirlotapide

Dir-loe'ta-pyed

**Trade and other names:** Slentrol

**Functional classification:** Obesity medication

## Pharmacology and Mechanism of Action

Dirlotapide is used to produce weight loss in dogs. It is related to another medication used for obesity in dogs, mitratapide (Yarvitan), which is approved in Europe. Dirlotapide is an inhibitor of the microsomal triglyceride transfer protein (MTP). The inhibition is selective, and the liver form of MTP is not affected in dogs. Inhibition of this enzyme reduces the ability of intestinal enterocytes to process triglycerides by preventing uptake of lipids into cholemicrons. As a result, there is decreased fat absorption and increased fecal fat. The accumulation of these triglycerides in the intestinal cells sends a signal (satiety messenger) to the CNS to suppress the appetite. In dogs, the effect on the intestinal cells reduces the uptake of dietary lipids in association with decreased postprandial serum triglycerides, phospholipids, and cholesterol. The weight loss is attributed to the reduced appetite rather than impaired processing of dietary lipids. It does not produce a direct centrally acting effect. Bioavailability of oral dirlotapide is variable but in the range of 20%-40%, with a volume of distribution (VD) of 1.3 L/kg. It is highly protein bound. Administration with food increases absorption. The plasma half-life is variable (1.2-11 hours). The effects on the intestinal cells and appetite appear to be local (intestinal) rather than attributed to plasma levels because similar weight reduction effects are not observed when dirlotapide is administered by injection.

## Indications and Clinical Uses

Dirlotapide is used in the management of obesity in dogs. During the treatment protocol, there is a consistent weight loss (approximately 3% per month) that is primarily

fat tissue, not lean tissue. Overall, the entire treatment period may result in weight loss of 18%-22% of body weight, but response can vary among individual dogs. Dirlotapide should not be used without instituting the proper protocol as outlined by the sponsor. It should be used in an overall weight management program, which also includes appropriate dietary changes. Before using to treat overweight or obesity, rule out other diseases such as hypothyroidism or hyperadrenocorticism.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects are proportional to dose. Decreased appetite occurs as a mode of action of the drug. Vomiting may also occur as a common effect related to the drug's mechanism of action. Nausea and diarrhea also may occur. None of these signs are necessarily cause to stop the medication and may resolve with time.

However, if vomiting and nausea persist, evaluation and adjustment of dose may be necessary. Changes in liver enzymes also are expected. There may be increases in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) liver enzymes associated with treatment. However, if there are high increases in ALT or marked elevation in other values (AST, gamma-glutamyl transpeptidase [GGT], alkaline phosphatase, or total bilirubin), treatment should be stopped and the patient reassessed. There may be decreased absorption of fat-soluble vitamins A and E. The reduced absorption of these vitamins has not been clinically significant.

#### **Contraindications and Precautions**

Do not administer to cats. Do not use in dogs with concurrent liver disease or dogs on long-term corticosteroid therapy. Humans should not take this drug. Safety in pregnancy has not been established.

#### **Drug Interactions**

No drug interactions have been reported. It has been safely administered with NSAIDs and ACE inhibitors.

### **Instructions for Use**

Feed a complete diet when using this medication. There is a specific protocol (see [dosing](#) section) that must be followed for proper use of this drug. Protocol follows an initial weight loss phase, usually 4 weeks; an adjustment phase of variable duration; and by a weight management phase of 12 weeks. The entire protocol may comprise 26 weeks. If reductions in diet are not maintained and diet is not restricted, animals may regain weight following cessation of treatment. To avoid rebound weight gain, continue feeding the maintenance diet amount identified during the posttreatment phase. Dirlotapide may be given directly in the mouth or with food. The appetite suppression is less in dogs that are fed a low-fat diet.

### **Patient Monitoring and Laboratory Tests**

Monitor patient's weight. Monitor blood chemistry profile for changes in liver enzymes and reduced albumin and electrolytes.

### **Formulations**

- Dirlotapide is available in a 5-mg/mL solution in medium-chain triglyceride (MCT) oil.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Once opened, it has a shelf-life of 3 months. Do not refrigerate.

## Small Animal Dosage

### Dogs

- Initial dose is 0.05 mg/kg (0.01 mL/kg), then increased to 0.1 mg/kg (0.02 mL/kg) at 14 days. Thereafter, the dose is adjusted monthly on the basis of weight loss in each individual dog. The maximum dose is 1.0 mg/kg (0.2 mL/kg).

### Cats

- Do not use in cats.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food.

## Disopyramide

dye-soe-peer'ah-mide

**Trade and other names:** Norpace (Rythmodan in Canada)

**Functional classification:** Antiarrhythmic agent

## Pharmacology and Mechanism of Action

Antiarrhythmic agent of Class I. Disopyramide blocks the inward sodium channel and depresses myocardial electrophysiologic conduction rate.

## Indications and Clinical Uses

Disopyramide is used for control of ventricular arrhythmias. Its use in veterinary medicine is not as common as for other drugs. Studies of efficacy in animals have not been reported.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. High doses may cause cardiac arrhythmias.

#### Contraindications and Precautions

At high doses, it may induce arrhythmias in some patients.

#### Drug Interactions

No drug interactions are reported for animals. Use cautiously with other drugs that may affect the cardiac rhythm.

## Instructions for Use

Disopyramide is not commonly used in veterinary medicine because of its short half-life in dogs. Other antiarrhythmic drugs are preferred.

## Patient Monitoring and Laboratory Tests

Monitor ECG in treated animals. This drug can be proarrhythmogenic.

### Formulations

- Disopyramide is available in 100- and 150-mg capsules and 10-mg/mL injection (Canada only).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Compounded oral formulations have been stable for 30 days.

### Small Animal Dosage

#### Dogs

- 6-15 mg/kg q8h PO.

#### Cats

- No dose established.

### Large Animal Dosage

- No use in large animals is reported.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Dithiazanine Iodide

dye-thye-az'ah-neen eye'oe-dide

**Trade and other names:** Dizan

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Microfilaricidal drug for dogs. It is also active against hookworms, roundworms, and whipworms.

### Indications and Clinical Uses

Dithiazanine is used to eliminate heartworm microfilaria in dogs. It also has been used to treat some intestinal parasites. The filaricidal activity of the macrocyclic lactones (ivermectin and related drugs) has replaced drugs such as dithiazanine. Instead of using dithiazanine for microfilaricidal treatment, the American Heartworm Society recommends the use of macrocyclic lactones.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are rare. Vomiting is reported in some dogs. Dithiazanine causes discoloration of feces.

#### Contraindications and Precautions

Do not use in animals with reduced renal function. Do not administer to heartworm-positive dogs until 6 weeks after adulticide therapy has been given.

#### Drug Interactions

No specific drug interactions have been reported.

### Instructions for Use

Administer with food. If powder is used, mix with food as top dressing. Before other drugs were available, this was the only microfilaricidal agent for dogs. However, with

improved availability and efficacy of other drugs such as the macrocyclic lactones, the use has diminished significantly.

### Patient Monitoring and Laboratory Tests

Monitor heartworm status after a course of therapy by checking for microfilaria.

### Formulations

- Dithiazanine is rarely available in commercial tablets any longer. Older formulations included 10-, 50-, 100-, and 200-mg tablets and 200-mg per tablespoon powder.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- Heartworm: 6.6-11 mg/kg q24h for 7-10 days PO.
- Roundworms: 22 mg/kg once daily for 3-5 days PO.
- Hookworms: 22 mg/kg once daily for 7 days PO.
- Whipworms: 22 mg/kg once daily for 10-12 days PO.

#### Cats

- No dose has been reported.

### Large Animal Dosage

- No use in large animals has been reported.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Dobutamine Hydrochloride

doe-byoo'tah-meen hye-droe-klor'ide

**Trade and other names:** Dobutrex

**Functional classification:** Cardiac inotropic agent

### Pharmacology and Mechanism of Action

Adrenergic agonist. Dobutamine is a racemic mixture (R and S isomers) that has both  $\beta_1$ - and  $\beta_2$ -adrenergic activity. However, its clinical effects are caused by the relative cardioselective agonist activity on  $\beta_1$  receptors. There are both agonist and antagonist effects on  $\alpha$ -receptors, the clinical effects of which are uncertain. The primary advantage of dobutamine is that it produces positive inotropic effects without excessive tachycardia. The lack of tachycardia distinguishes it from other sympathomimetic agents. At appropriate infusion rates, dobutamine can improve contractility without increasing heart rates. Dobutamine has a short half-life in animals (2-3 minutes). Therefore it must be given via constant IV infusion and has a short onset of activity.

### Indications and Clinical Uses

Dobutamine is used primarily for the acute treatment of heart failure. It produces an inotropic effect without increasing heart rate. Short treatment regimens (e.g., 48 hours) can have a residual positive effect in some animals.

**Precautionary Information****Adverse Reactions and Side Effects**

Dobutamine may cause tachycardia and ventricular arrhythmias at high doses or in sensitive individuals. If tachycardia or arrhythmias are detected, stop infusion rate and resume at a lower rate.

**Contraindications and Precautions**

Do not use in animals with ventricular arrhythmias.

**Drug Interactions**

Do not mix with alkaline solutions, such as those containing bicarbonate. Do not infuse in IV line with heparin, cephalosporins, or penicillins. Otherwise, it is compatible with most fluid solutions. Do not administer to animals receiving monoamine oxidase inhibitors (MAOIs) (e.g., selegiline).

**Instructions for Use**

Dobutamine has a rapid elimination half-life (minutes) and therefore must be administered via carefully monitored CRI. Dose rates (infusion rate) can be adjusted by monitoring patient response. In dogs, doses as low as 2 mcg/kg/min have improved cardiac output.

**Patient Monitoring and Laboratory Tests**

Monitor heart rate and ECG during treatment. Cardiac arrhythmias are possible during infusions, especially at high doses.

**Formulations**

- Dobutamine is available in a 250-mg/20 mL (12.5-mg/mL) vial for injection.

**Stability and Storage**

Usually dilute in 5% dextrose solution (e.g., 250 mg in 1 L 5% dextrose). A slight pink tinge to the solution can occur without loss of potency; however, do not use if color turns brown.

**Small Animal Dosage****Dogs**

- 5-20 mcg/kg/min IV infusion. Generally start with low dose and titrate upward.

**Cats**

- 2 mcg/kg/min IV infusion.

**Large Animal Dosage****Horses**

- 5-10 mcg/kg/min (0.005-0.01 mg/kg/min) IV infusion. Observe for increases in heart rate and ventricular arrhythmias. Adjust dose as needed based on patient response and heart rate.

**Regulatory Information**

No regulatory information is available. Because of a short half-life, no risk of residue is anticipated in food animals.

RCI Classification: 3

## Docusate

dok'yoo-sate

**Trade and other names:** Docusate calcium: Surfak and Doxidan; Docusate sodium: DSS, Colace, and Doxan, and generic brands

**Functional classification:** Laxative

D

### Pharmacology and Mechanism of Action

Docusate sodium and docusate calcium are stool softeners. They act as surfactants to help increase water penetration into feces. They act to decrease surface tension to allow more water to accumulate in the stool.

### Indications and Clinical Uses

Docusate is indicated for medical conditions in which softened feces are desirable, such as after intestinal or anal surgery, to help pass hardened feces, and when administering drugs that slow intestinal transit (e.g., opiates). Docusate is indicated for treatment of constipation.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse effects reported in animals. In people, high doses have caused abdominal discomfort.

#### Contraindications and Precautions

Some formulations of docusate calcium and docusate sodium products have contained the stimulant cathartic phenolphthalein, which should be used cautiously in cats. Examine label of products to ensure absence of phenolphthalein.

#### Drug Interactions

No specific drug interactions are reported for animals.

### Instructions for Use

Doses are based on extrapolations from humans or empiricism. No clinical studies reported for animals.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Docusate calcium is available as 60-mg tablets and 240-mg capsules.
- Docusate sodium is available as 50- and 100-mg capsules and 10-mg/mL liquid.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- Docusate calcium: 50-100 mg/dog q12-24h PO.
- Docusate sodium: 50-200 mg/dog q8-12h PO.

#### Cats

- Docusate calcium: 50 mg/cat q12-24h PO.
- Docusate sodium: 50 mg/cat q12-24h PO.



**Large Animal Dosage**

- Docusate sodium: 10 mg/kg/day PO.

**Regulatory Information**

No regulatory information is available for animals intended for food. Because docusate has primarily a local acting effect in the intestine, there is a minimal risk of residues in animals intended for food.

**Dolasetron Mesylate**

doe-lah'seh-tron mess'ih-late (also, dahl-AH-set-rahn)

**Trade and other names:** Anzemet

**Functional classification:** Antiemetic

**Pharmacology and Mechanism of Action**

Antiemetic drug from the class of drugs called *serotonin antagonists*. These drugs act by inhibiting serotonin (5-HT, type 3) receptors. During chemotherapy, there may be 5-HT released from injury to the GI tract, which stimulates vomiting centrally. The emetic response induced by serotonin is inhibited by this class of drugs. In people, dolasetron is completely metabolized to hydrodolasetron (active), which is presumably the same active metabolite for dogs and cats. Serotonin antagonists used for antiemetic therapy include granisetron, ondansetron, dolasetron, and tropisetron.

**Indications and Clinical Uses**

Like other serotonin antagonists, dolasetron is used primarily for its antiemetic effects during chemotherapy, for which they generally have been superior to other drugs in efficacy. These drugs also may be used to control vomiting from surgery (postoperative nausea and vomiting).

**Precautionary Information****Adverse Reactions and Side Effects**

Dolasetron adverse effects have not been reported in animals. These drugs have little affinity for other 5-HT receptors. Some effects may be indistinguishable from concurrent cancer drugs.

**Contraindications and Precautions**

There are no important contraindications identified in animals.

**Drug Interactions**

No drug interactions are reported. However, dolasetron is subject to effects from cytochrome P450 inducers and inhibitors. (See Appendixes H and I.)

**Instructions for Use**

Dolasetron has been used infrequently in veterinary medicine because of its expense. Doses are derived from anecdotal experience or extrapolation from human studies, and no clinical studies are reported from animal studies. These drugs are more effective if used to prevent vomiting (administered prior to a chemotherapeutic agent) rather than to treat ongoing vomiting. This class of drugs may be combined with corticosteroids (e.g., dexamethasone) to enhance the antiemetic action.

**Patient Monitoring and Laboratory Tests**

Monitor GI signs in vomiting patient.

## Formulations

- Dolasetron is available in 50- and 100-mg tablets and 20-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It may be added to fluid solutions (compatible in most IV fluid solutions), but do not mix with other IV drugs. Do not use injection after 24 hours when added to fluids. Oral formulations have been added to fruit juice up to 2 hours at room temperature without loss of stability.

## Small Animal Dosage

### Dogs and Cats

- Prevention of nausea and vomiting: 0.6 mg/kg, q12-24h, IV, SQ, or PO, or 1.2 mg/kg once.
- Treating vomiting and nausea: 1 mg/kg once daily IV or PO.

## Large Animal Dosage

- No dose has been reported.

## Regulatory Information

Use in animals intended for food is negligible. No regulatory information is available.

## Domperidone

dahm-pare'ih-done

**Trade and other names:** Motilium and Equidone Gel

**Functional classification:** Prokinetic agent

## Pharmacology and Mechanism of Action

Domperidone is a motility modifier once used in people, but withdrawn because of cardiac arrhythmias. It has actions similar to metoclopramide, although it is chemically unrelated. A difference between metoclopramide and domperidone is that the latter does not cross the blood-brain barrier. Therefore, adverse CNS effects are not as much of a problem with domperidone. Domperidone stimulates motility of the upper GI tract, probably through dopaminergic effects or by increasing acetylcholine effects. The action of domperidone is to inhibit dopamine receptors and enhance the action of acetylcholine in GI tract. Domperidone will also have endocrine effects by stimulating secretion of prolactin. There is preliminary evidence that domperidone, via alpha-adrenergic and serotonergic blocking properties, may prevent vasoconstriction and reduction in laminar blood flow in horses with laminitis. The pharmacokinetics in horses show that absorption is low (1.2-1.5%), which may limit use for some indications.

## Indications and Clinical Uses

In horses, it is approved for prevention of fescue toxicosis in periparturient mares. In horses, domperidone has been used to treat fescue toxicosis and periparturient agalactia. Fescue toxicosis is caused by a fungus that produces a toxin that causes reproductive problems in horses. The action of domperidone to increase lactation is through the stimulation of prolactin. It increases follicular growth in seasonally anestrus mares and has been used (with altrenogest and estradiol) to induce lactation in barren mares. Domperidone as a dopamine antagonist also has been used for testing for pituitary pars intermedia dysfunction (PPID) in horses.

Domperidone has been used to treat gastroparesis and treatment of vomiting. However, at a dose of 1.1 mg/kg oral in horses, it did not produce a significant

intestinal motility stimulating effect; but, at 0.2 mg/kg IV it was effective at restoring motility in experimental horses (no IV form is available).

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects that are seen with metoclopramide are not as common with domperidone because it does not cross the blood-brain barrier as readily as metoclopramide. It causes a transient increase in aldosterone and prolactin secretion. It has also caused a transient increase in plasma adrenocorticotrophic hormone (ACTH), which could exacerbate equine Cushing syndrome.

#### Contraindications and Precautions

Do not use in patients with gastrointestinal obstruction.

#### Drug Interactions

Acidity is needed for oral administration. Do not administer with stomach antacids such as omeprazole, cimetidine, or antacids, or acid suppressing drugs such as omeprazole, or H-2 receptor blockers (e.g., famotidine).

### Instructions for Use

Domperidone has questionable efficacy as a prokinetic agent for treatment of ileus in animals. The equine gel is available for use in horses for treatment of agalactia and fescue toxicosis.

### Patient Monitoring and Laboratory Tests

No specific monitoring is required, but clinical monitoring of GI motility is important.

### Formulations

- Formulation used in horses is oral gel at 11% (110 mg/mL). In Canada, it is available as 10-mg tablets for people.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

- Doses for small animals have not been established, but 2-5 mg per dog or cat q8-12h PO (0.05-0.1 mg/kg) has been used.

### Large Animal Dosage

#### Horses

- For fescue toxicity and agalactia: Equidone oral gel (11%) administered 10 days prior to foaling at 1.1 mg/kg daily PO, starting 10 days before the scheduled foaling date. (This dose is equivalent to 5 mL per 500 kg or 5 mL per adult horse daily PO of the 11% oral gel.) Continue until foaling. If there is not adequate milk production after foaling, continue for 5 additional days.

For testing horses with suspect PPID: Administer 5 mg/kg oral domperidone and collect blood samples at 0, 2, 4, hours for endogenous ACTH measurement. The ACTH reference range is 9-35 pg/mL.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Dopamine Hydrochloride

doe'pah-meen hye-droe-klor'ide

**Trade and other names:** Intropin (discontinued), and generic

**Functional classification:** Cardiac inotropic agent

**D**

### Pharmacology and Mechanism of Action

Adrenergic and dopamine agonist. Dopamine is a neurotransmitter and an immediate precursor to norepinephrine. At low doses it stimulates the dopamine (DA<sub>1</sub>) receptors, at moderate doses it stimulates the adrenergic receptors, and at high doses it acts as an alpha<sub>1</sub>-receptor agonist (producing vasoconstriction). At doses that stimulate DA<sub>1</sub> receptors, it increases cAMP in smooth muscle cells and causes relaxation and vasodilation. It has been administered to stimulate the heart and to increase urine flow (see next for explanation of renal effects).

### Indications and Clinical Uses

Dopamine is used therapeutically to stimulate myocardium via action on cardiac beta<sub>1</sub>-receptors. Dopamine infusions will increase both blood pressure and cardiac output. These effects are caused by stimulating cardiac contractility and heart rate by acting as an agonist for beta<sub>1</sub>-adrenergic receptors. In addition, dopamine increases the release of norepinephrine from nerve terminals (dopamine is a precursor for norepinephrine). It produces a greater chronotropic effect than dobutamine. It has been proposed that dopamine dilates renal arterioles, increases renal blood flow, and increases the glomerular filtration rate. This effect is proposed to occur via activation of renal dopamine-1 (DA<sub>1</sub>) receptors. Because of this proposed effect, in the past it has been used for acute renal failure. However, recent evaluation has raised doubts about the clinical effectiveness of dopamine for treatment of acute renal failure. Cats do not have as many DA<sub>1</sub> receptors as other animals; therefore it has not been effective in cats to produce diuresis. In addition, evaluation in people and other animals has not produced desired effects. Therefore, there is little support for the use of dopamine to treat acute kidney disease in animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Dopamine may cause tachycardia and ventricular arrhythmias at high doses or in sensitive individuals.

#### Contraindications and Precautions

Dopamine is unstable in alkaline fluids.

#### Drug Interactions

Do not mix with alkaline solutions. Otherwise, it is compatible with most fluid solutions.

### Instructions for Use

Dopamine has a rapid elimination half-life (minutes) and therefore must be administered via carefully monitored CRI. Because the actions of dopamine are dose dependent, the rate administered is adjusted to reach the desired clinical effect. Dopamine has been administered at doses of 2-10 mcg/kg/min for the acute management of heart failure and cardiogenic shock. When preparing IV solutions, one may admix 200-400 mg of dopamine with 250-500 mL of fluid. Dopamine is unstable in alkaline fluid solutions, such as those containing bicarbonate.

Low dose (vasodilation, D<sub>1</sub> receptor): 0.5-2 mcg/kg/min; medium dose (cardiac stimulating, beta<sub>1</sub>-receptor): 2-10 mcg/kg/min; and high dose (vasoconstriction, alpha-receptors) : >10 mcg/kg/min.

### **Patient Monitoring and Laboratory Tests**

Monitor heart rate and rhythm while administering dopamine.

### **Formulations**

- Dopamine is available in 40-, 80-, and 160-mg/mL for IV injection.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. It may be added to fluids such as 5% dextrose, saline, and lactated Ringer's solution. It is stable for 24 hours after dilution. Do not use if solution turns a brown or purple color.

### **Small Animal Dosage**

#### **Dogs and Cats**

- 2-10 mcg/kg/min IV infusion. Dose rate is dependent on desired effects.

### **Large Animal Dosage**

#### **Horses and Cattle**

- 1-5 mcg/kg/min IV infusion.

### **Regulatory Information**

No regulatory information is available. Because of a short half-life, no risk of residue is anticipated in food animals.

RCI Classification: 2

## **Doramectin**

dore-ah-mek'tin

**Trade and other names:** Dectomax

**Functional classification:** Antiparasitic

### **Pharmacology and Mechanism of Action**

Antiparasitic drug. Avermectins (ivermectinlike drugs) and milbemycins (milbemycin, doramectin, and moxidectin) are macrocyclic lactones and share similarities, including mechanism of action. These drugs are neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Paralysis and death of the parasite is caused by increased permeability to chloride ions and hyperpolarization of nerve cells. These drugs also potentiate other chloride channels, including ones gated by GABA. Mammals ordinarily are not affected because they lack glutamate-gated chloride channels, and there is a lower affinity for other mammalian chloride channels. Because these drugs ordinarily do not penetrate the blood-brain barrier, GABA-gated channels in the CNS of mammals are not affected. Therefore it produces longer and more sustained plasma concentrations. It is effective against nematodes and arthropods, but has no effect on flukes or tapeworms.

### **Indications and Clinical Uses**

Doramectin is used for treatment or prevention of GI parasite (nematode) infections in livestock, lice infestation, lungworm infection, and treatment of scabies. There are

reports of a single injection (200-300 mcg/kg) used in cats for treatment of notoedric mange (infections from the mite *Notoedres cati*).

### Precautionary Information

#### Adverse Reactions and Side Effects

Toxicity may occur at high doses and in breeds in which ivermectinlike drugs cross the blood-brain barrier. Sensitive breeds include collies, Australian shepherds, Shetland sheepdogs, and Old English sheepdogs. Toxicity is neurotoxic, and signs include depression, ataxia, impaired vision, coma, and death. Sensitivity to ivermectinlike drugs may be because of mutation in the blood-brain barrier (p-glycoprotein deficiency). Treatment of hypodermal larvae in cattle may elicit reactions in tissues from dead larvae. These drugs are safe for pregnant animals. No adverse effects were seen in cats treated with doses as high as 345 mcg/kg.

#### Contraindications and Precautions

Doramectin is only approved in cattle. Certain breeds of dogs (Shetland sheepdogs and collie-type breeds) are more sensitive to adverse effects than other breeds.

#### Drug Interactions

Use cautiously with drugs that may inhibit p-glycoprotein at the blood-brain barrier (see Appendix J).

### Instructions for Use

Doses vary depending on use. In cattle, treatment of hypodermal larvae should begin at the end of fly season. Administration to cattle should use a 16- or 18-gauge needle for SQ administration. For IM injection, use a 1.5-inch needle and inject in the neck muscle. When administering the topical form, remove mud and manure from hide. If it rains within 2 hours of administration, decreased efficacy may occur.

### Patient Monitoring and Laboratory Tests

Monitor for microfilaremia prior to administration in small animals.

### Formulations

- Doramectin is available in a 1% (10-mg/mL) injection and a 5-mg/mL (0.5%) topical transdermal solution.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- Demodex treatment: 600 mcg/kg/wk for 5-23 weeks SQ.

#### Cats

- Mite infection: 200-270 mcg/kg once SQ.
- 0.1 mL of 1% solution given once SQ.

### Large Animal Dosage

#### Cattle

- 200 mcg/kg (0.2 mg/kg) or 1 mL per 50 kg (110 pounds), single injection, IM or SQ.
- Transdermal solution: Give 500 mcg (0.5 mg) per kg or 1 mL per 10 kg (4.5 pounds) as a single dose along the animal's back, along the midline.

**Pigs**

- 300 mcg/kg (0.3 mg/kg) or 1 mL per 34 kg (75 pounds), single injection, IM.

**Regulatory Information**

Cattle withdrawal time (meat): 35 days.

Pig withdrawal time (meat): 24 days.

Do not administer to lactating dairy cattle.

Do not administer to female dairy cattle older than 20 months of age.

Cattle transdermal solution withdrawal time (meat): 45 days. Do not administer to lactating dairy cattle; do not administer within 2 months of calving.

**Doripenem**

dor-i-pen'em

**Trade and other names:** Doribax

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Beta-lactam antibiotic of the carbapenems class with broad spectrum of activity. Action on cell wall is similar to other beta-lactams, which is to bind penicillin-binding proteins (PBPs) that weaken or interfere with cell wall formation. In *Escherichia coli* and *Pseudomonas aeruginosa*, doripenem binds to PBP 2, which is involved in the maintenance of cell shape, and to PBPs 3 and 4. Carbapenems have a broad spectrum of activity and are among the most active of all antibiotics. Doripenem has similar activity as imipenem and meropenem to include gram-negative bacilli, including *Enterobacteriaceae* and *P. aeruginosa*. It is slightly more active against *P. aeruginosa*. It also is active against most gram-positive bacteria, except methicillin-resistant strains of *Staphylococcus*. It is not active against *Enterococcus*.

**Indications and Clinical Uses**

Doripenem is indicated primarily for resistant infections caused by bacteria resistant to other drugs. It is especially valuable for treating resistant infections caused by *P. aeruginosa*, *E. coli*, and *Klebsiella pneumoniae*. Doripenem is not used in veterinary medicine as commonly as meropenem or imipenem.

**Precautionary Information****Adverse Reactions and Side Effects**

Carbapenems pose similar risks as other beta-lactam antibiotics, but adverse effects are rare. Doripenem does not cause seizures as frequently as imipenem.

**Contraindications and Precautions**

Some slight yellowish discoloration may occur after reconstitution. Slight discoloration will not affect potency. However, a darker amber or brown discoloration may indicate oxidation and loss of potency.

**Drug Interactions**

Do not mix in vial or syringe with other antibiotics or with solutions containing other drugs.

**Instructions for Use**

Doses in animals have been based on pharmacokinetic studies rather than efficacy trials. To prepare IV injection, mix 500-mg vial with 10 mL of sterile water for

injection or sodium chloride 0.9% injection, gently shaking vial to form a suspension (concentration, 50 mg/mL). Withdraw suspension and add to infusion bag containing normal saline 100 mL or dextrose 5%, gently shaking until clear (concentration, 4.5 mg/mL). To prepare 250-mg dose, mix with 10 mL of sterile water for injection or sodium chloride 0.9% injection, gently shaking vial to form a suspension (concentration, 50 mg/mL). Withdraw suspension and add to infusion bag containing normal saline 100 mL or dextrose 5%, gently shaking until clear (concentration, 4.5 mg/mL). Remove 55 mL of this solution from bag and discard. Infuse remaining solution (concentration, 4.5 mg/mL).

### Patient Monitoring and Laboratory Tests

Susceptibility testing: Use susceptibility to imipenem to guide testing for doripenem. Enteric gram-negative bacteria usually have MIC values less than 0.5 mcg/mL.

*P. aeruginosa* usually have MIC values less than 2.0 mcg/mL.

### Formulations

- Doripenem is available in a 500-mg vial for injection.

### Stability and Storage

Store vial at 59° F to 86° F. Constituted suspension in vial may be stored for 1 hour prior to dilution in infusion bag. Infusion solution prepared in saline may be stored at room temperature for 8 hours (includes infusion time) or under refrigeration for 24 hours (includes infusion time). Infusion solution prepared in dextrose 5% may be stored at room temperature for 4 hours (includes infusion time) or under refrigeration for 24 hours.

### Small Animal Dosage

#### Dogs and Cats

- 8 mg/kg q8h IV. Infuse over 30 minutes to 1 hour.

### Large Animal Dosage

- No large animal doses have been reported. However, doses similar to the range used in small animals are suggested for foals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Doxapram Hydrochloride

doks'ah-pram hye-droe-klor'ide

**Trade and other names:** Dopram, Respiram

**Functional classification:** Respiratory stimulant

### Pharmacology and Mechanism of Action

Respiratory stimulation of doxapram results from direct stimulation of the medullary respiratory center and activation of the aortic and carotid body chemoreceptors to improve sensitivity to carbon dioxide. These receptors are sensitive to changes in CO<sub>2</sub>, which in turn stimulate the respiratory center. Doxapram is used primarily in emergency during anesthesia or to decrease the respiratory depressant effects of certain drugs (e.g., opiates, barbiturates). An important use in veterinary medicine is



stimulation of respiration in young horses. The half-life is short (2 hours), but the duration of action is only 5-10 minutes after IV administration.

### **Indications and Clinical Uses**

Doxapram may stimulate respiration in dogs, cats, and horses during and after general anesthesia. It has been used to stimulate respiration in newborn animals following dystocia or cesarean section surgery. Doxapram will increase ventilation (tidal volume, respiratory rate) and reduce acidosis. In horses, it will cause cardiac stimulation and respiratory stimulation. There have been reports that administration to neonates may increase their suckling activity shortly after birth and subsequently decrease the incidence of failure of passive transfer of immunoglobulins. The primary use of doxapram in horses is for the treatment of respiratory acidosis in foals caused by hypoxic-ischemic encephalopathy (perinatal asphyxia or neonatal maladjustment syndrome) in neonatal foals. Administration to foals has restored normal ventilation and improved blood pH, PaO<sub>2</sub>, and respiratory rate in neonatal foals in a dose-dependent manner. Doxapram also has been used in dogs to assist in the diagnosis of laryngeal paralysis.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects have not been reported in animals. CNS stimulation and excitement are possible with high doses or rapid infusions.

#### **Contraindications and Precautions**

Do not use in animals with cardiac or respiratory arrest. Do not use with positive pressure ventilation.

#### **Drug Interactions**

Use with theophylline or aminophylline may increase CNS excitement.

### **Instructions for Use**

Doxapram has a rapid onset of effect (usually occurs in 20-40 seconds with peak effect at 1-2 minutes) and a short duration of action. The duration of effect varies from 5-12 minutes. Treatment guidelines have been developed primarily for foals. Single-dose injections may be administered, followed by CRIs.

### **Patient Monitoring and Laboratory Tests**

Monitor patient's heart and respiratory rate.

### **Formulations**

- Doxapram is available in a 20-mg/mL solution.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. The pH is 3.5-5 for IV administration, which may affect compatibility with other drugs. Stability of compounded formulations has not been evaluated.

### **Small Animal Dosage**

- 5-10 mg/kg IV.
- Neonate: 1-5 mg SQ, sublingual, or via umbilical vein.

### **Large Animal Dosage**

- Foals: initial IV dose of 0.5 mg/kg, followed by a CRI of 0.03-0.08 mg/kg/min for 20 minutes; or initiate treatment with 0.05-0.08 mg/kg/min CRI and continue for 8-12 hours.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

## Doxepin

doks'eh-pin

**Trade and other names:** Sinequan

**Functional classification:** Behavior-modifying drug, tricyclic antidepressant (TCA)

## Pharmacology and Mechanism of Action

Tricyclic antidepressant. For treatment of depression, this class of drugs is thought to act by increasing synaptic concentrations of norepinephrine and serotonin (5-HT) in the CNS. Doxepin is only a moderate to weak inhibitor of the reuptake of these neurotransmitters. It also has antihistamine ( $H_1$ ) properties.

## Indications and Clinical Uses

Doxepin has been used to treat anxiety disorders and dermatologic conditions in dogs and cats. Some use for dermatitis is related to the drug's antihistamine properties. Although it has been used for treating pruritus and dermatitis in small animals, it has not been effective for treating atopic dermatitis in dogs. Doxepin has been used to treat lick granuloma in dogs. There are anecdotal reports of the use of doxepin for treating laryngeal paralysis in dogs, but no controlled studies to support this use.

## Precautionary Information

### Adverse Reactions and Side Effects

Tricyclic antidepressants have some antimuscarinic effects that may increase heart rate, cause xerostomia, and affect the GI tract. Some sedation is possible with doxepin.

### Contraindications and Precautions

As with other TCAs, do not administer with other antidepressant drugs. Use cautiously in patients with glaucoma or seizure disorders.

### Drug Interactions

Doxepin may increase sedative effects from antihistamines. Do not administer with MAOIs.

## Instructions for Use

Doxepin has primarily been administered to treat pruritus in dogs. The efficacy for this use has been disappointing.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Doxepin is available in 10-, 25-, 50-, 75-, 100-, and 150-mg capsules and 3- and 6-mg tablets (Silenor). Generic and Sinequan are available in a 10-mg/mL oral solution.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Oral formulations can be mixed with various flavorings, juices, and foods without loss of stability.

**Small Animal Dosage****Dogs**

- 1-5 mg/kg q12h PO. Start with low dose (for example, 0.5-1 mg/kg) and gradually increase.
- Lick granuloma: 0.5-1 mg/kg q12h PO. (For comparison, antipruritic dose for people is 10-25 mg/person one to three times per day and increased as needed.)

**Cats**

- 0.5-1 mg/kg q12-24h. Start with low dose initially.

**Large Animal Dosage**

- No large animal doses are reported.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

**Doxorubicin Hydrochloride**

doks-oh-roo'bih-sin hye-droe-klor'ide

**Trade and other names:** Adriamycin

**Functional classification:** Anticancer agent

**Pharmacology and Mechanism of Action**

Anticancer agent. Doxorubicin is derived from the soil fungus *Streptomyces peucetius*. Doxorubicin damages DNA by inhibition of the enzyme topoisomerase II. This enzyme is responsible for DNA functions. When topoisomerase is inhibited, the DNA segments cannot perform transcription, leading to breaks in the DNA strands and cell death. Secondly, this mechanism causes cell death by blocking synthesis of RNA and proteins. Doxorubicin also forms free radicals (OH) that can attack DNA and lead to oxidation of DNA. In dogs, the half-life has varied from 8.7-11 hours, with VD 0.6-0.7 L/kg and clearance 52-83 L/kg/hr. In cats, the pharmacokinetics are highly variable, with half-lives ranging from 11 minutes to 9.5 hours. Other anti-tumor antibiotics include mitoxantrone, actinomycin D, and bleomycin.

**Indications and Clinical Uses**

Doxorubicin is used for treatment of various neoplasias, including hemangiosarcoma and lymphoma. Doxorubicin is commonly used in humans for the treatment of breast tumors, various sarcomas, and osteosarcoma. In veterinary medicine, it has been used for lymphoma, osteosarcoma, and other carcinomas and sarcomas. Response for T-cell lymphoma is significantly less than for B-cell lymphoma in dogs. It is considered one of the most effective single agents in the treatment of lymphoma. It is used commonly in cancer protocols with other agents. In limited studies in horses, it was highly effective for treatment of some tumors (lymphoma, carcinoma, and sarcoma) as a single agent.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects limit the frequency and cumulative doses that can be administered. Bone marrow toxicity is the major adverse effect that limits the frequency of acute administration, and the cardiotoxicity is the major effect that limits the chronic administration. The nadir of bone marrow depression (leukopenia) is at 7-10 days. The stem cells are usually spared, and recovery occurs within 21 days following each dose. Cardiac toxicity is caused by an acute effect during administration seen as arrhythmias and decreased systolic function and a chronic effect that manifests as cardiomyopathy and congestive heart failure. Cardiac toxicity is caused by production of reactive oxygen species that injure cardiac myocytes, or blockage of topoisomerase type 2-beta, which leads to mitochondrial dysfunction. Cardiac toxicity is dose related. The risk of chronic effects increases as total cumulative doses exceed 200-240 mg/m<sup>2</sup>. In some dogs, cardiac changes can be observed as soon as after 120 mg/m<sup>2</sup> cumulative dose. Dexrazoxane (Zincard) is a potent chelator of iron and has been used to decrease the adverse cardiac effects in some patients. Alopecia is common in people, but primarily is seen only in dogs that have continuously growing hair (e.g., poodles). Cats may lose their whiskers. Gastrointestinal acute side effects—anorexia, vomiting, and diarrhea—were the most common acute side effects. Hypersensitivity (allergic) reactions are not life threatening, but they can occur commonly. They are probably not true allergic reactions, but are simply the result of mast cell degranulation that occurs independently of immunoglobulin G (IgG) binding. Signs of this reaction are head shaking (ear pruritus) and generalized urticaria and erythema. Cats are more sensitive to adverse effects than dogs, so lower doses are used in cats. Adverse effects in cats include anorexia, vomiting, and renal injury. In horses, adverse effects included bone marrow suppression, hair loss, dermatitis, and other skin reactions.

Local reactions may occur if the extravasation of injectable dose is observed. If this occurs, flush the area to dilute the drug. Dexrazoxane may be used to decrease local reaction caused by extravasation by administering 500 mg/m<sup>2</sup> within 6 hours of extravasation. Local treatments also may be needed.

### Contraindications and Precautions

Do not use in animals with cardiomyopathy. Monitor CBC in patients before and after treatment. If significant leukopenia (particularly neutropenia of fewer than 1000 cells) is present, withhold treatment or use a lower-dose intensity. Use cautiously in dogs with known mutation deficiency in the MDR membrane transporter (p-glycoprotein) (e.g., collies and related breeds). These dogs are more prone to toxicity.

### Drug Interactions

Doxorubicin is commonly administered with other anticancer drugs, antiemetics, and antihistamines without adverse effects. However, doxorubicin is a p-glycoprotein substrate and should not be used with drugs that are p-glycoprotein inhibitors (e.g., cyclosporine or ketoconazole). (See Appendix J for list of inhibitors.)

## Instructions for Use

Regimen listed may differ for various tumors. To prepare solution, the total dose is diluted in a saline fluid solution of 25 or 50 mL and infused slowly over 20-30 minutes, but preferably over 60 minutes. Extending duration of infusion to 2-3 hours may decrease some adverse effects. For cats, mix 1 mg/mL in saline solution and administer IV over 5-10 minutes with fluids. In cats, SQ fluids (22 mL/kg) may be

administered with doxorubicin. This drug is very irritating, and special care must be made to ensure that extravasation from the vein does not occur. For canine lymphoma, some oncologists believe that remission of cancer is best achieved when five treatments are administered (target 150-180 mg/m<sup>2</sup> cumulative dose). In chemotherapy protocols, it is sometimes administered with cyclophosphamide. Animals may require antiemetic and antihistamine (diphenhydramine) prior to therapy. Most often, it is administered on a body surface area rate (mg/m<sup>2</sup>); however, dose according to body weight (mg/kg) may be safer for small dogs (see “[Small Animal Dosage](#)” section). In cats, additional SQ fluids are administered to prevent renal toxicity.

### Patient Monitoring and Laboratory Tests

Monitor ECG during therapy. Electrocardiograms should be performed periodically in dogs to look for evidence of myocardial toxicity. Complete blood count should be monitored regularly and prior to each treatment because of risk of myelotoxicity.

### Formulations

- Doxorubicin is available in a 2-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 30 mg/m<sup>2</sup> q21days IV.
- Dogs >15 kg body weight: 30 mg/m<sup>2</sup>.
- Dogs <15 kg body weight: 1 mg/kg.

#### Cats

- 20 mg/m<sup>2</sup> (approximately 1.25 mg/kg) q3wks IV. In some cats, higher doses of 25 mg/m<sup>2</sup> appear to be equally tolerated.

### Large Animal Dosage

#### Horses

- 70 mg/m<sup>2</sup>, (0.84-0.96 mg/kg) IV every 3 weeks for 6 cycles.

### Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Doxycycline Hyclate, Doxycycline Monohydrate

doks-ih-sye'kleen

**Trade and other names:** Vibramycin, Monodox, Doxy Caps, and generic brands

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Tetracycline antibiotic. Mechanism of action of tetracyclines is to bind to the 30S ribosomal subunit and inhibit protein synthesis. The action of tetracyclines is usually bacteriostatic. It has a broad spectrum of activity, including bacteria, some protozoa, *Rickettsia*, and *Ehrlichia*. In dogs, after oral administration the half-life is 12.6 hours, the volume of distribution is 1.7 L/kg and oral absorption is 66%, producing a peak

concentration of 4.5 mcg/mL. In horses, 10 mg/kg intragastric had a half-life of 13.8 hours with oral absorption of 17%, and a peak concentration of 0.48 mcg/mL.

## Indications and Clinical Uses

Doxycycline is usually the drug of choice for treating tickborne diseases in animals. Efficacy has been demonstrated in research studies and in some clinical studies. It is used for treating infections caused by bacteria, some protozoa, *Rickettsia*, and *Ehrlichia*. Doxycycline administered to cats with infections caused by *Mycoplasma* or *Chlamydophila felis* (formerly *Chlamydia psittaci*) at 10-15 mg/kg once daily PO, or 5 mg/kg q12h PO, has been effective in eliminating the organism and improving clinical signs. In dogs, 5 mg/kg q12h PO for 3-4 weeks has cleared *Ehrlichia canis* from blood and tissues. Doxycycline is recommended by the American Heartworm Society to be added to treatment of canine heartworm disease. It is used for heartworm disease because of the activity against the organism *Wolbachia*. This may improve microfilaricidal effect when combined with ivermectin, improve response to adjuvant treatment with melarsomine, and decrease injury to pulmonary vessels. In horses, it has been used to treat ehrlichiosis, but also has been used to treat other diseases (e.g., respiratory infections) when oral treatment is indicated. In recent years, doxycycline has become unavailable or more expensive. If other oral alternatives are needed, minocycline hydrochloride is an acceptable substitute (see *minocycline* section for more details).

## Precautionary Information

### Adverse Reactions and Side Effects

Tetracyclines may cause renal tubular necrosis at high doses and can affect bone and teeth formation in young animals. However, doxycycline has not been reported to cause the problems with chelation to calcium and teeth discoloration in animals. Doxycycline administered orally to cats has caused esophageal irritation, tissue injury, and esophageal stricture. This may be caused by solid-dose formulations (primarily doxycycline hyclate rather than doxycycline monohydrate) becoming entrapped in the esophagus. Passage into the stomach by giving the cat water or food after administration is advised to prevent this effect. Doxycycline given IV to horses has been fatal; however, it has been administered safely to horses PO, although diarrhea is possible. In two equine studies there were no adverse effects reported from oral administration. In another study, one of the horses in a pharmacokinetic trial developed signs of enteritis and colic.

### Contraindications and Precautions

Ordinarily tetracyclines should not be administered to young animals because it can affect bone and teeth formation. However, it has been better tolerated in children than other tetracyclines. If solid-dose forms are administered to cats, lubricate the tablet/capsule, or follow with food or water to ensure passage into stomach. Do not administer rapidly IV. Do not administer solution IM or SQ. Do not administer IV to horses under any circumstances; acute death has been reported from this use.

Tetracyclines bind to compounds containing calcium, which decreases oral absorption. However, this is less of a problem with doxycycline than with other tetracyclines. Doxycycline has been mixed with milk prior to oral administration to children without decreasing efficacy.

## Instructions for Use

Many pharmacokinetic and experimental studies have been conducted in small animals. Doxycycline is ordinarily considered the drug of choice for *Rickettsia* and

*Ehrlichia* infections in dogs. Doxycycline is more effective than enrofloxacin for *Ehrlichia*. When used with ivermectin (6 mcg/kg weekly) for heartworm treatment, doxycycline was administered at a dose of 10 mg/kg per day intermittently for several months (e.g., 20 months out of 36 months). To prepare doxycycline IV infusion solution, add 10 mL to a 100-mg vial or 20 mL to a 200-mg vial and then further dilute for IV use in 100 to 1000 mL of lactated Ringer's solution or 5% dextrose. Infuse over 1 to 2 hours (see "[Stability and Storage](#)" section).

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are  $\leq 0.25$  mcg/mL for testing isolates from dogs. Breakpoints for cats are not established, but similar values are recommended. Tetracycline can be used as the class representative for susceptibility to doxycycline. Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline or minocycline or both.

### Formulations

- Doxycycline is available in a 10-mg/mL oral suspension, 50-, 75-, 100-, and 150-mg tablets, and 50- and 100-mg capsules (doxycycline hyclate). Doxycycline monohydrate is available as 50- or 100-mg tablets or capsules. A controlled-release formulation (Oracea) contains 10-mg delayed release and 30-mg immediate release in one capsule. Doxycycline hyclate injection is available in a 100- and 200-mg injection vial.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Avoid mixing with cations such as iron, calcium, aluminum, and zinc. However, doxycycline tablets have been mixed with milk and immediately administered to children without loss of potency. Doxycycline hyclate for injection will retain potency for 12 hours at room temperature or 72 hours refrigerated after reconstitution at concentrations up to 1 mg/mL. IV solutions are stable in lactated Ringer's solution or 5% dextrose for 6 hours at room temperature. Protect IV solutions from light. If frozen after reconstitution with sterile water, solutions of 10 mg/mL are potent for 8 weeks. Doxycycline calcium or doxycycline monohydrate commercial suspension for people is stable for two weeks at room temperature, if stored in light-resistant container after reconstitution with water. Doxycycline tablets may be crushed and mixed with food, drinks (milk or pudding), and are stable for 24 hours at room temperature. If doxycycline is prepared in a compounded formulation, it may be unstable. Doxycycline hyclate formulated in Ora Plus and Ora Sweet as a suspension retained potency for only 14 days. Other suspensions prepared for animals also may be unstable. Observe for dark color change (dark brown) as evidence of loss of potency. When doxycycline hyclate and doxycycline monohydrate was compounded in an oil-based suspension, it was stable for 180 days. However the suspension precipitates in the container and vigorous mixing is suggested prior to administration.

### Small Animal Dosage

#### Dogs and Cats

- 5 mg/kg q12h PO or IV. 10 mg/kg q24h PO.
- *Rickettsia* (dogs): 5 mg/kg q12h.
- *Ehrlichia* (dogs): 5 mg/kg q12h for at least 14 days.
- Hemoplasmosis (cats): 10 mg/kg, PO, once daily for 7 days.
- Heartworm treatment (dogs): 10 mg/kg q12h, PO, administered for 28 days prior to adulticide treatment. It may be administered in combination with ivermectin.

**Birds**

- Mix four 100-mg doxycycline hyclate capsules with 1 L water (400 mg/L). Shake to make solution and offer as only source of water to birds to eliminate bacteria. Alternatively, 25 mg/kg PO q12h for 3 weeks.

**Large Animal Dosage**

- Dose: 10-20 mg/kg q12h PO. For *Lawsonia intracellularis*: 20 mg/kg PO q24h for 3 weeks.
- Horses: 10-20 mg/kg q12h PO. The higher dose of 20 mg/kg is recommended for most bacterial infections. For *Lawsonia intracellularis*: 20 mg/kg PO, q24h, for 3 weeks.
- Horses: Do not administer IV.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Dronabinol**

droe-nab'ih-nole

**Trade and other names:** Marinol

**Functional classification:** Antiemetic

**Pharmacology and Mechanism of Action**

Antiemetic from the cannabinoid class. The site of action is unknown, but there is some evidence that the active ingredient may affect opiate receptors, or they may affect other receptors in the vomiting center. For dronabinol, the oral absorption is good, but bioavailability is low because of high first-pass effects. The volume of distribution is high.

**Indications and Clinical Uses**

Cannabinoids have been used in people who have not responded to any other antiemetic drugs (e.g., patients who are receiving anticancer drugs). They have also gained recent popularity to increase the appetite in patients with terminal disease, cancer, and AIDS. Their use has not been reported in veterinary patients, but they have been used by some veterinarians to increase the appetite in cats.

**Precautionary Information****Adverse Reactions and Side Effects**

Cannabinoids are relatively well tolerated in people, but side effects include drowsiness, dizziness, ataxia, and disorientation. Withdrawal signs may occur after abrupt discontinuation after repeated doses.

**Contraindications and Precautions**

No known contraindications.

**Drug Interactions**

No drug interactions reported for animals.



**Instructions for Use**

Dronabinol is a form of synthetic marijuana (tetrahydrocannabinol [THC]) and is available as an antiemetic prescription drug. Most clinical use in animals has been anecdotal. It has been administered to decrease vomiting and improve appetite associated with chemotherapy.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Dronabinol is available in 2.5-, 5-, and 10-mg capsules.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats**

- 5 mg/m<sup>2</sup> PO, up to 15 mg/m<sup>2</sup> for antiemetic administration prior to chemotherapy.
- Appetite stimulation: start at 2.5 mg before meals.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

Do not administer to animals intended for food.

## Edetate Calcium Disodium

ed'eh-tate kal'see-um dye-soe-dee-um

**Trade and other names:** Calcium disodium versenate and calcium disodium ethylenediaminetetra-acetate (EDTA)

**Functional classification:** Antidote

### Pharmacology and Mechanism of Action

Chelating agent. Readily chelates with lead, zinc, cadmium, copper, iron, and manganese.

### Indications and Clinical Uses

Edetate calcium disodium is indicated for treatment of acute and chronic lead poisoning. It is sometimes used in combination with dimercaprol.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse effects reported in animals. In people, allergic reactions (release of histamine) have occurred after intravenous (IV) administration.

#### Contraindications and Precautions

Do not use edetate disodium to substitute for edetate calcium disodium because it will chelate calcium in the patient.

#### Drug Interactions

No specific drug interactions are reported. However, it has the potential to chelate other drugs if mixed together.

### Instructions for Use

Edetate calcium disodium may be used with dimercaprol. It is equally effective when administered intravenously or intramuscularly, but intramuscular (IM) injection may be painful. Ensure adequate urine flow before the first dose is administered.

### Patient Monitoring and Laboratory Tests

Monitor lead concentrations to assess treatment.

### Formulations

- Edetate calcium disodium is available in a 200-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

- 25 mg/kg q6h for 2-5 days SQ, IM, or IV.

### Large Animal Dosage

- 25 mg/kg q6h for 2-5 days SQ, IM, or IV.

### Regulatory Information

Withdrawal time: 2 days for meat; 2 days for milk (extralabel).

## Edrophonium Chloride

ed-roe-foe'nee-um klor'ide

**Trade and other names:** Tensilon and generic brands

**Functional classification:** Antimyasthenic, anticholinesterase

### Pharmacology and Mechanism of Action

Cholinesterase inhibitor. Edrophonium causes cholinergic effects by inhibiting metabolism of acetylcholine. Its effects do not last long, and it is used for short-term use only.

### Indications and Clinical Uses

Because edrophonium is short acting, it ordinarily is only used for diagnostic purposes (e.g., myasthenia gravis). It also has been used to reverse neuromuscular blockade of nondepolarizing agents (pancuronium).

### Precautionary Information

#### Adverse Reactions and Side Effects

Edrophonium is short acting, and side effects are minimal. Overdose in nonmyasthenia animals may cause salivation, retching, vomiting, and diarrhea. If this is observed, administer atropine at 0.02-0.04 mg/kg. Excessive muscarinic/cholinergic effects may occur with high doses; these may also be counteracted with atropine.

#### Contraindications and Precautions

Edrophonium will potentiate effects of other cholinergic drugs. Cats are especially sensitive to edrophonium (see dose differences in “[Small Animal Dosage](#)” section).

#### Drug Interactions

Use cautiously with other cholinergic drugs.

### Instructions for Use

Edrophonium is used only for determination of diagnosis of myasthenia gravis. An alternative drug for this purpose is neostigmine methylsulfate (Prostigmin) at 40 mcg/kg IM or 20 mcg/kg IV.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Edrophonium is available in a 10-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 0.11-0.22 mg/kg IV (maximum dose is 5 mg per dog).

#### Cats

- 0.25-0.5 mg/cat IV.

### Large Animal Dose

- No large animal doses have been reported.

## Regulatory Information

No regulatory information is available. Because of a short half-life, no risk of residue is anticipated in food animals.

Racing Commissioners International (RCI) classification: 3

## Enalapril Maleate

eh-nal'ah-prill mal'ee-ate

**Trade and other names:** Enacard (veterinary preparation) and Vasotec (human preparation)

**Functional classification:** Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

## Pharmacology and Mechanism of Action

Angiotensin-converting enzyme inhibitor. Like other ACE inhibitors, it inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and will also stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The ability of aldosterone to cause sodium and water retention contributes to congestion.

Enalapril, like other ACE inhibitors, will cause vasodilation and decrease aldosterone-induced congestion, but ACE inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins.

## Indications and Clinical Uses

Enalapril, like other ACE inhibitors, is used to treat hypertension and congestive heart failure (CHF). Efficacy for treating CHF has been established from clinical trials and can be used with other drugs such as pimobendan, furosemide, digoxin, and spironolactone. It is primarily used in dogs. In addition to its use for treatment of CHF, enalapril has been used to delay onset of CHF in dogs with mitral regurgitation. The benefit of enalapril and other ACE inhibitors for occult heart disease is controversial; some studies have shown a benefit and others have not. Enalapril has been used in some cats in heart failure or with systemic hypertension. Unfortunately, approximately 50% of cats with hypertension do not respond to enalapril, and ACE inhibitors are not considered a primary treatment for hypertension in cats.

Angiotensin-converting enzyme inhibitors also have been shown to be beneficial in the management of certain types of kidney disorders (nephropathy) and for renal hypertension. Renal benefits result from limiting systemic and glomerular capillary hypertension, the antiproteinuric effect to decrease in urine protein-to-creatinine ratio, and retarding the development of glomerular sclerosis and tubulointerstitial lesions. Angiotensin-converting enzyme inhibitors have decreased proteinuria in patients, but long-term benefits on survival have not been established. The benefits of ACE inhibitor treatment in cats with chronic renal disease are somewhat modest and have little effect on survival time or long-term prognosis.

Large animal uses have not been established, but in horses the metabolite enalaprilat at 0.5 mg/kg IV completely inhibited ACE activity, but did not change blood pressure or other hemodynamic variables in response to exercise.

**Precautionary Information****Adverse Reactions and Side Effects**

Enalapril may cause azotemia in some patients; carefully monitor patients receiving high doses of diuretics.

**Contraindications and Precautions**

Discontinue ACE inhibitors in pregnant animals; they cross the placenta and have caused fetal malformations and death of the fetus.

**Drug Interactions**

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease vasodilating effects.

**Instructions for Use**

Doses are based on clinical trials conducted in dogs. For dogs, generally start with once-daily administration and increase to q12h if needed (see [dosing](#) section). In some dogs with mild disease, start with 0.25 mg/kg q12h, then increase to 0.5 mg/kg q12h at the first recheck. Other drugs used for treatment of heart failure, such as pimobendan, may be used concurrently.

**Patient Monitoring and Laboratory Tests**

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

**Formulations**

- Enalapril is available as Vasotec (human preparation) in 2.5-, 5-, 10-, and 20-mg tablets and as Enacard (veterinary preparation) in 1-, 2.5-, 5-, 10-, and 20-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Enalapril, compounded in a variety of oral suspensions and flavorings, was stable for 60 days. Above pH of 5, degradation occurs more quickly.

**Small Animal Dosage****Dogs**

- 0.5 mg/kg q12-24h PO. In some animals it may be necessary to increase dose to 1 mg/kg per day, administered as 0.5 mg/kg q12h.

**Cats**

- 0.25-0.5 mg/kg q12-24h PO.
- 1-1.25 mg/cat/day PO.

**Large Animal Dosage**

- There are no clinical studies available to establish doses for horses.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

RCI classification: 3

## Enflurane

en-floor'ane

**Trade and other names:** Ethrane

**Functional classification:** Inhalant anesthetic

### Pharmacology and Mechanism of Action

Inhalant anesthetic. Like other inhalant anesthetics, the mechanism of action is uncertain. Enflurane produces a generalized, reversible, depression of the CNS. The inhalant anesthetics vary in their solubility in blood, their potency, and the rate of induction and recovery. Those with low blood/gas partition coefficients are associated with the most rapid rates of induction and recovery. Enflurane has a vapor pressure of 175 mm Hg (at 20° C), a blood/gas partition coefficient of 1.8, and a fat/blood coefficient of 36.

### Indications and Clinical Uses

Enflurane, like other inhalant anesthetics, is used for general anesthesia in animals. It has a minimum alveolar concentration (MAC) value of 2.37%, 2.06%, and 2.12% in cats, dogs, and horses, respectively.

### Precautionary Information

#### Adverse Reactions and Side Effects

Like other inhalant anesthetics, enflurane produces vasodilation and increased blood flow to cerebral blood vessels. This may increase intracranial pressure. Like other inhalant anesthetics, it produces a dose-dependent myocardial depression with accompanying decrease in cardiac output. It also depresses respiratory rate and alveolar ventilation. Like other inhalant anesthetics, it increases the risk of ventricular arrhythmias, especially in response to catecholamines.

#### Contraindications and Precautions

No specific contraindications are reported for animals.

#### Drug Interactions

Other sedatives and anesthetics (e.g., opiates, benzodiazepines, phenothiazines, alpha-2 agonists) will lower the requirement for inhalent gas anesthesia.

### Instructions for Use

Titrate dose for each individual with anesthetic monitoring.

### Patient Monitoring and Laboratory Tests

Monitor anesthesia parameters. During anesthesia, monitor heart rate and rhythm and respiratory rate.

### Formulations

- Enflurane is available as a solution for inhalation.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

- Induction: 2%-3%.
- Maintenance: 1.5%-3%.

## Large Animal Dosage

- MAC value: 1.66%.

## Regulatory Information

No withdrawal times are established for food animals. Clearance is rapid, and short withdrawal times are suggested. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Enilconazole

en-il-kah'nah-zole

**Trade and other names:** Imaverol and Clinafarm-EC

**Functional classification:** Antifungal

## Pharmacology and Mechanism of Action

Azole antifungal agent for topical use only. Like other azoles, enilconazole inhibits membrane synthesis (ergosterol) in fungus and weakens the cell wall. It is highly active against dermatophytes.

## Indications and Clinical Uses

Enilconazole is only used topically. It is used as a topical agent for treatment of dermatophytes; as a spray, it is used to treat the environment. It may be applied to animal bedding, stalls, and cages. In addition to dermatologic use, enilconazole has been instilled into the nasal sinuses of dogs for treatment of nasal aspergillosis.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects have not been reported. However, it is reported that if used on cats, they should be prevented from licking fur after application until the drug has dried.

### Contraindications and Precautions

No specific contraindications are reported.

### Drug Interactions

No specific interactions are reported. However, like other azoles, systemic treatment may result in cytochrome P450 enzyme inhibition.

## Instructions for Use

It is only used topically. Imaverol is available in Canada as 10% emulsion. In the US, Clinafarm EC is available for use in poultry units as 13.8% solution. Dilute solution to at least 50:1 and apply topically every 3-4 days for 2-3 weeks. Enilconazole also has been instilled as 1:1 dilution into the nasal sinus for nasal aspergillosis. In addition, enilconazole has been used in a diluted form as a spray to kill fungi on bedding, equine tack, and cages.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations Available

- Enilconazole is available as 10% or 13.8% emulsion.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. When the emulsion is mixed, it should be used immediately and not stored.

## Small Animal Dosage

- Nasal aspergillosis: 10 mg/kg q12h instilled into nasal sinus for 14 days (10% solution diluted 50/50 with water).
- Dermatophytes: dilute 10% solution to 0.2% and wash lesion with solution four times at 3- to 4-day intervals. Solution may be sponged directly on animal. Allow solution to air dry.

## Large Animal Dosage

### Horses

- Dilute 10% solution to 0.2% and wash lesions with solution four times at 3- to 4-day intervals.
- Treatment of aspergillus rhinitis: infuse in nasal catheter a 2% solution every 12 hours (25-100 mL).

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Enoxaparin Sodium

en-oks'ah-pare-in

**Trade and other names:** Lovenox and low-molecular-weight heparin (LMWH)

**Functional classification:** Anticoagulant

## Pharmacology and Mechanism of Action

Low-molecular-weight heparin is also known as *fragmented heparin*. Low-molecular-weight heparin is characterized by a molecular weight composed of approximately 5000, compared to conventional heparin (unfractionated) with a molecular weight of approximately 15,000. Subsequently, the absorption, clearance, and activity of LMWH differ from unfractionated heparin (UFH). Low-molecular-weight heparins produce their effect by binding to antithrombin (AT) and increasing antithrombin III-mediated inhibition of synthesis and activity of coagulation factor Xa. However, LMWH, unlike conventional heparin, produces less inhibition of thrombin (factor IIa). Low-molecular-weight heparin's activity is described by the anti-factor Xa/anti-factor IIa ratio. Enoxaparin has a ratio of 3.8:1 (the conventional UFH ratio is 1:1). In people, LMWHs have several advantages compared to UFH and include greater anti-Xa/IIa activity, more complete and predictable absorption from injection, longer duration, less frequent administration, reduced risk of bleeding, and a more predictable anticoagulant response. However, in dogs and cats, the half-life of LMWH is much shorter than in humans, reducing some of this advantage. In dogs, the half-life of enoxaparin is approximately 5 hours; in cats, it is estimated to be 1.9 hours, which requires much more frequent administration in either species to maintain anti-Xa activity compared to humans. Low-molecular-weight heparins used in veterinary medicine include tinzaparin (Innohep), enoxaparin (Lovenox), and dalteparin (Fragmin). In people, enoxaparin has replaced dalteparin as the preferred LMWH for clinical use.



## Indications and Clinical Uses

Enoxaparin, like other LMWHs, is used to treat hypercoagulability disorders and prevent coagulation disorders such as thromboembolism, venous thrombosis, disseminated intravascular coagulopathy (DIC), and pulmonary thromboembolism. Clinical indications are derived from uses of conventional heparin or extrapolated from human medicine. There have been few clinical studies to examine efficacy of LMWH in animals. Previously published doses extrapolated from humans have been shown *not* to produce adequate and consistent anti-Xa activity in dogs and cats; therefore, specific doses for dogs and cats, rather than extrapolated from human medicine, should be used.

### Precautionary Information

#### Adverse Reactions and Side Effects

Although better tolerated than regular heparin, bleeding is a risk. However, LMWHs produce fewer bleeding problems than administration of conventional heparin. Low-molecular-weight heparins are associated with a lower incidence of heparin-induced thrombocytopenia in people, but heparin-induced thrombocytopenia from any form of heparin has not been a clinical problem in animals. If excessive anticoagulation and bleeding occur as a result of an overdose, protamine sulfate should be administered to reverse heparin therapy. The protamine dose is 1.0 mg protamine for every 1.0 mg enoxaparin administered by slow IV infusion. Protamine complexes with heparin to form a stable, inactive compound.

#### Contraindications and Precautions

Do not administer IM to prevent hematoma; administer SQ only. Low-molecular-weight heparin is excreted by renal clearance in animals; therefore if renal disease is present, the elimination will be prolonged. Rebound hypercoagulability may occur after discontinuation of heparin treatment; therefore it may be advised to taper the dose slowly when discontinuing treatment.

#### Drug Interactions

Do not mix with other injectable drugs. Use cautiously in animals that are already receiving other drugs that can interfere with coagulation, such as aspirin and warfarin. Although a specific interaction has not been identified, use cautiously in animals that may be receiving certain chondroprotective compounds such as glycosaminoglycans for treatment of arthritis. Some antibiotics, such as cephalosporins, may inhibit coagulation.

## Instructions for Use

Dosing recommendations extrapolated from human medicine are not appropriate for animals. Animal owners should be warned that LMWHs are expensive compared to conventional heparin. When dosing, do not interchange doses on a unit-for-unit basis with heparin or other LMWHs because they differ in manufacturing process, molecular weight distribution, anti-Xa and anti-IIa activities, units, and dosage.

## Patient Monitoring and Laboratory Tests

Monitor patients for clinical signs of bleeding problems. When administering LMWH, activated partial thromboplastin time (aPTT) and prothrombin time (PT) clotting times are not reliable indicators of therapy, although prolonged aPTT is a sign of overdosing. Anti-Xa activity is considered the preferred laboratory measure of LMWH activity in people, but the use of this parameter is controversial in animals. Peak anti-Xa activity occurs 3-4 hours after dosing, and the target range for anti-Xa activity should be 0.5-1.0 U/mL for cats and 0.5-2.0 U/mL for dogs.

## Formulations

- Enoxaparin is available as 100 mg/mL in the following sizes: 30 mg in 0.3-mL, 40 mg in 0.4-mL, 60 mg in 0.6-mL, 80 mg in 0.8-mL, 100 mg in 1-mL and 300 mg per 3 mL injection; and 150 mg/mL with 120 mg per 0.8 mL and 150 mg/mL injection

## Stability and Storage

Store in a tightly sealed container protected from light. The pH of the injection is 5.5-7.5.

## Small Animal Dosage

### Dogs

- 0.8 mg/kg SQ q6h (see monitoring section for dose adjustment).

### Cats

- 1 mg/kg SQ q12h, up to 1.25 mg/kg SQ q6h (see monitoring section for dose adjustment).

## Large Animal Dosage

### Horses

- Prophylaxis: 0.5 mg/kg q24h SQ and 1 mg/kg q24h SQ for high-risk patients.

## Regulatory Information

Extralabel withdrawal times are not established. However, 24-hour withdrawal times are suggested because this drug has little risk from residues.

## Enrofloxacin

en-roe-floks'ah-sin

**Trade and other names:** Baytril and generic

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Fluoroquinolone antibacterial drug. Enrofloxacin acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. It is a bactericidal with a broad spectrum of activity. In most animal species, enrofloxacin is metabolized, at least partially, to ciprofloxacin. Ciprofloxacin is an active desmethyl metabolite of enrofloxacin and may contribute in an additive fashion to the antibacterial effects. At the peak concentration, ciprofloxacin may account for approximately 10% and 20% of the total concentration in cats and dogs, respectively. Susceptible bacteria include *Staphylococcus*, *Escherichia coli*, *Proteus*, *Klebsiella*, and *Pasteurella*. *Pseudomonas aeruginosa* is moderately susceptible, but requires higher concentrations. Enrofloxacin has poor activity against *Streptococcus* and anaerobic bacteria.

## Indications and Clinical Uses

Enrofloxacin, like other fluoroquinolones, is used to treat susceptible bacteria in a variety of species. Treatment has included infections of skin and soft tissue, urinary tract infections in dogs and cats, *Chlamydomydia felis* infections in cats, and ulcerative colitis caused by *Escherichia coli* in dogs. Enrofloxacin has been shown effective for treating *Rickettsia* infections in dogs. However, it is not effective for treating *Ehrlichia* (see Doxycycline). In horses, it has been used for a variety of soft tissue infections and respiratory infections, although this use is based primarily on anecdotal experience. Enrofloxacin is approved for the treatment and control of swine respiratory disease (SRD) associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis*, and *Streptococcus suis*. It is also approved for

treatment of bovine respiratory disease (BRD) associated with *Mannheimia haemolytica*, *P. multocida*, and *Haemophilus somni* (previously *Haemophilus somnus*). Enrofloxacin is also used in most exotic animal species because of its safety and activity against a wide variety of pathogens.

## **Precautionary Information**

### **Adverse Reactions and Side Effects**

High concentrations may cause central nervous system (CNS) toxicity, especially in animals with renal failure. It may cause occasional vomiting and, at high doses, may cause some nausea and diarrhea. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4 weeks to 28 weeks of age. Large, rapidly growing dogs are the most susceptible. Cats are relatively resistant to cartilage injury, but foals are susceptible. Blindness in cats that is caused by retinal degeneration has been reported. Affected cats have had permanent blindness. This may be a dose-related effect. Cats administered doses of 20 mg/kg developed retinal degeneration, but did not at 5 mg/kg. Therefore dose restrictions in cats have been used. Administration of concentrated solution (100 mg/mL) given orally to horses has caused oral mucosal lesions. When injected, this solution (pH 10.5) may be irritating to some tissues.

### **Contraindications and Precautions**

Avoid use in young dogs because of risk of cartilage injury. Do not administer to young foals; injury to articular cartilage has been reported. Use cautiously in animals that may be prone to seizures, such as epileptics. Do not administer to cats at doses greater than 5 mg/kg/day.

### **Drug Interactions**

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum, magnesium (for example, antacids), iron, and calcium, may decrease absorption. Sucralfate suspension, but not intact tablets, may inhibit oral absorption because aluminum chelates with enrofloxacin.

Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur. Enrofloxacin may precipitate in an IV line if injected directly into IV fluids.

## **Instructions for Use**

A low dose of 5 mg/kg/day is used for sensitive organisms with minimum inhibitory concentration (MIC) values of 0.12 mcg/mL or less or urinary tract infection. A dose of 5-10 mg/kg/day is used for organisms with MIC of 0.12-0.5 mcg/mL (e.g., gram-positive bacteria). A dose of 10-20 mg/kg/day is used for organisms with MIC of 0.5-1.0 mcg/mL (e.g., *P. aeruginosa*). The solution is not approved for IV use, but it has been administered via this route safely if given slowly. Enrofloxacin was not absorbed in cats after transdermal application in a pluronic gel vehicle. Concentrated enrofloxacin solution (cattle formulation at 100 mg/mL) is basic (pH 10.5); therefore it can be irritating to some animals when injected intramuscularly. Do not inject more than 20 mL at each site. Also, this formulation may precipitate out of solution if pH is decreased by other solutions.

## **Patient Monitoring and Laboratory Tests**

Susceptibility testing: For small animals, Clinical and Laboratory Standards Institute (CLSI) break points for sensitive organisms are  $\leq 0.5$  mcg/mL. Minimum inhibitory concentration values  $\geq 4$  are considered resistant. If MIC values are 1 or 2 mcg/mL,

higher doses may be justified. For cattle, the break point for sensitive organisms is  $\leq 0.25$  mcg/mL. Other fluoroquinolones may be used in some cases to estimate susceptibility to this fluoroquinolone, but a test using a specific drug is recommended. Ciprofloxacin break points for susceptibility testing are not equivalent because they were derived from human use. Enrofloxacin may cause a false-positive result on urine glucose tests when using a tablet (e.g., ClinTest) copper reduction test.

### Formulations

Enrofloxacin is available in 22.7- and 68-mg tablets; Taste Tabs are 22.7, 68, and 136 mg. It is also available in a 22.7-mg/mL injection and a 100-mg/mL preparation for large animals (Baytril-100).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has been evaluated, and it was found to be stable with many mixtures. A 1% solution diluted in other vehicles (chlorhexidine, salicylic acid, EDTA, and water) was stable for 28 days. However, do not mix with solutions that contain ions that may chelate with enrofloxacin (iron, magnesium, aluminum, and calcium). If administered intravenously, it is recommended to first dilute the solution in fluids (e.g., 1:10 dilution) and infuse slowly. The 100-mg/mL solution is alkaline and contains benzyl alcohol and L-arginine as a base (pH 10). The pH of this solution is alkaline and, if lowered, it may precipitate. The 22.7-mg/mL formulation has a pH of 11.5 and may not be compatible with some solutions.

### Small Animal Dosage

#### Dogs

- 5-20 mg/kg/day IM, PO, or IV.  
For uncomplicated lower urinary tract infection, 18-20 mg/kg once daily PO every 3 days.

#### Cats

- 5 mg/kg/day PO or IM. (Avoid IV use in cats.)

#### Exotic Animals

- Usually 5 mg/kg/day IM or oral in reptiles every other day.

#### Birds

- 15 mg/kg q12h IM or PO.

### Large Animal Dosage

#### Horses

- 5 mg/kg q24h IV.
- 7.5-10 mg/kg q24h PO.
- 5 mg/kg of 100 mg/mL solution (Baytril-100) IM, once per day (rotate injection sites).

#### Cattle (BRD)

- Single dose: 7.5-12.5 mg/kg once SQ (3.4-5.7 mL per 100 pounds).
- Multiple-dose: 2.5-5 mg/kg SQ (1.1-2.3 mL per 100 pounds) once daily for 3-5 days.

#### Swine (SRD)

- 7.5 mg/kg SQ, behind the ear, once.

### Regulatory Information

Cattle withdrawal time: 28 days for meat. Not to be used in lactating dairy cattle or calves intended to be used as veal. Do not use in female dairy cattle 20 months of age or older. Pig withdrawal time: 5 days.

Extralabel use of fluoroquinolones in animals that produce food is illegal.

## Ephedrine Hydrochloride

eh-fed'rin hye-droe-klor'ide

**Trade and other names:** Generic brands

**Functional classification:** Adrenergic agonist

### Pharmacology and Mechanism of Action

Adrenergic agonist. Decongestant. Ephedrine acts as an agonist on alpha-adrenergic receptors and beta<sub>1</sub>-adrenergic receptors, but has less effect on beta<sub>2</sub> receptors.

### Indications and Clinical Uses

Ephedrine is used as a vasopressor (e.g., when it is administered during anesthesia). It also has been used as a CNS stimulant. Oral formulations have been used to treat urinary incontinence because of action on bladder sphincter muscle. However, this is no longer recommended, and most oral dose forms are no longer available.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are related to excessive adrenergic activity (e.g., peripheral vasoconstriction and tachycardia).

#### Contraindications and Precautions

Use in animals with cardiovascular disease is not recommended.

#### Drug Interactions

No specific drug interactions are reported. However, ephedrine will potentiate any other adrenergic agonist.

### Instructions for Use

The most current use is from injection primarily in acute situations to increase blood pressure. Oral use for urinary incontinence in dogs has diminished because of lack of available formulations.

### Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm in patients.

### Formulations

- **Most formulations of ephedrine have been removed from the market.** Previously available as a 25- and 50-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- Urinary incontinence: 4 mg/kg or 12.5-50 mg/dog q8-12h PO.
- Vasopressor: 0.75 mg/kg IM or SQ, repeat as needed.

#### Cats

- Urinary incontinence: 2-4 mg/kg q12h PO.
- Vasopressor: 0.75 mg/kg IM or SQ, repeat as needed.

### Large Animal Dosage

- No large animal doses are reported.

## Regulatory Information

Withdrawal time: No withdrawal times are established. Ephedrine is metabolized after administration, and a short withdrawal is recommended.

RCI classification: 2

## Epinephrine

eh-pih-nef'rin

**Trade and other names:** Adrenaline and generic brands

**Functional classification:** Adrenergic agonist

## Pharmacology and Mechanism of Action

Adrenergic agonist. Epinephrine nonselectively stimulates alpha-adrenergic and beta-adrenergic receptors. The alpha-adrenergic effects will increase vascular resistance and act as a potent vasopressor. The beta<sub>2</sub>-adrenergic effects will increase bronchodilation and decrease inflammatory mediators in the airways. Epinephrine is a potent adrenergic agonist with a prompt onset and a short duration of action. Compared to norepinephrine, epinephrine has more profound beta-receptor activity. As a result, compared to norepinephrine, epinephrine is more likely to cause increases in heart rate and tachyarrhythmias than norepinephrine.

## Indications and Clinical Uses

Epinephrine is used primarily for emergency situations to treat cardiopulmonary arrest and anaphylactic shock. It is administered IV, IM, or endotracheal for acute use. Vasopressin (arginine vasopressin) has replaced epinephrine as a vasopressor in some cardiopulmonary resuscitation (CPR) protocols. Epinephrine has been used in horses to test for diagnosis of anhidrosis, but terbutaline sulfate challenge is used more frequently for this test.

## Precautionary Information

### Adverse Reactions and Side Effects

Overdose will cause excessive vasoconstriction and hypertension. High doses can cause ventricular arrhythmias. When high doses are used for cardiopulmonary arrest, an electrical defibrillator should be available.

### Contraindications and Precautions

Avoid repeated administration in patients.

### Drug Interactions

Epinephrine will interact with other drugs that are used to either potentiate or antagonize alpha-adrenergic or beta-adrenergic receptors. It is incompatible with alkaline solutions (e.g., bicarbonate), chlorine, bromine, and salts of metals or oxidizing solutions. Do not mix with bicarbonates, nitrates, citrates, and other salts.

## Instructions for Use

Doses are based on experimental studies, primarily in dogs. Clinical studies are not available. Intravenous doses are ordinarily used, but endotracheal administration is acceptable when intravenous access is not available. When the endotracheal route is used, the dose is higher (up to 10 times the IV dose for CPR) and duration of effect

may be longer than with IV administration. When administering doses endotracheally, one can dilute the dose in a volume of 2-10 mL of saline. The intraosseous route also has been used, and doses are equivalent to IV doses. There appears to be no advantage to intracardiac injection compared to IV administration. Solutions are available in 1:1000 and 1:10,000 (either 1 mg/mL or 0.1 mg/mL). Generally, only the 1:10,000 solution is given IV. 1:1000 solutions are intended for IM use. Avoid the SQ route of administration because the vasoconstriction produced will delay absorption from this site.

For CPR, the doses have been controversial (see [dosing](#) section). There is a low dose (10 mcg/kg or 0.01 mg/kg) and a high dose (100 mcg/kg or 0.1 mg/kg). Generally, start with the low dose every 3-5 minutes IV in CPR, then use the high dose after prolonged CPR.

### **Patient Monitoring and Laboratory Tests**

Monitor heart rate and rhythm during treatment.

### **Formulations**

- Epinephrine is available in a 1-mg/mL (1:1000) injection solution and 0.1-mg/mL (1:10,000) injection solution. The 1:10,000 is most often used IV, and the 1:1000 solution is used IM or SQ. Ampules for people are designed to deliver 1 mg/person (approximately 14 mcg/kg).

### **Stability and Storage**

It is compatible with plastic in syringes. When solution becomes oxidized, it turns brown. Do not use if this color change is observed. It is most stable at pH of 3-4. If pH of solution is >5.5, it becomes unstable.

### **Small Animal Dosage**

- Cardiac arrest: 10-20 mcg/kg IV or 100-200 mcg/kg (0.1-0.2 mg/kg) endotracheal (may be diluted in saline before administration).
- Anaphylactic shock: 5-10 mcg/kg IV or IM, or 50 mcg/kg endotracheal (may be diluted in saline).
- Vasopressor therapy: 100-200 mcg/kg (0.1-0.2 mg/kg) IV (high dose) or 10-20 mcg/kg (0.01-0.02 mg/kg) IV (low dose). Administer low dose first, and if no response use high dose.
- Constant-rate infusion (CRI): 0.05 mcg/kg/min IV.
- During emergency use, the dose may be repeated every 5-15 minutes, but maximum dose in dogs is 0.3 mg total for dogs less than 40 kg, and 0.5 mg total for dogs greater than 40 kg body weight.

### **Large Animal Dosage**

- 1 mg/mL (1:1000) solution most often used.
- Anaphylactic shock (cattle, pigs, horses, and sheep): 20 mcg/kg (0.02 mg/kg) IM or 1 mL per 45 kg (1 mL per 100 pounds). 5-10 mcg/kg (0.005-0.01 mg/kg) IV or 0.25-0.5 mL per 45 kg (100 pounds).

### **Regulatory Information**

No withdrawal times are established. Epinephrine is rapidly metabolized after administration, and 0 days is recommended for withdrawal.

RCI classification: 2

## Epoetin Alfa (Erythropoietin)

ee-poe'eh-tin

**Trade and other names:** Procrit, Eprex, and Erythropoietin

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Human recombinant erythropoietin. Hematopoietic growth factor that stimulates erythropoiesis.

### Indications and Clinical Uses

Epoetin alfa is used to treat nonregenerative anemia. It has been used to treat myelosuppression caused by disease or chemotherapy. It also has been used to treat chronic anemia associated with chronic renal failure. The value of epoetin alfa to improve anemia in cats with chronic renal failure has been established in several studies. In some animals, anemia is also caused by iron deficiency and can be combined with ferrous sulfate at a dose of 50-100 mg per cat daily. Darbepoetin alfa (Aranesp), a similar drug, also has been used in small animals (see darbepoetin alfa section).

### Precautionary Information

#### Adverse Reactions and Side Effects

Because this product is a human-recombinant product, it may induce local and systemic allergic reactions in animals. Injection site pain and headache have occurred in people. Seizures also have occurred. Delayed anemia may occur because of cross-reacting antibodies against animal erythropoietin (reversible when drug is withdrawn). Antierythropoietin antibodies may increase with long-term use, which may occur in as high as 30% of treated cats, leading to failure of treatment.

#### Contraindications and Precautions

Stop therapy with epoetin when joint pain, fever, anorexia, or cutaneous reactions are observed.

#### Drug Interactions

No interactions are reported.

### Instructions for Use

The use of epoetin alfa has been limited primarily to dogs and cats. The only form currently available is a human-recombinant product. It is used in animals when hematocrit falls below 25%. In cats, 100 units/kg SQ three times a week is administered until a target hematocrit of 30%-40% is attained. Thereafter, twice-weekly injections are used. Maintenance dose is usually in a range of 75-100 units/kg SQ once or twice a week.

### Patient Monitoring and Laboratory Tests

Monitor hematocrit. Dose should be adjusted to maintain hematocrit in a range of 30%-34%.

### Formulations Available

- Epoetin alfa is available in a range of strengths, including 2,000-, 3,000-, 4,000-, 10,000-, 20,000-, and 40,000-units/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.



## Small Animal Dosage

### Dogs

- 35 or 50 units/kg three times a week, up to 400 units/kg/wk SQ (adjust dose to maintain hematocrit of 30%-34%).

### Cats

- Start with 100 units/kg SQ three times weekly; reduce to twice weekly and to once weekly when target hematocrit of 30%-40% is attained. In most cats, maintenance dose is 75-100 units/kg SQ twice weekly.

## Large Animal Dosage

- No large animal doses are reported.

## Regulatory Information

No withdrawal times are established for food animals. Erythropoietin in any form is prohibited to be on the premises of racing horses.

RCI classification: 2

## Epsiprantel

ep-sih-pran'til

**Trade and other names:** Cestex

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Anticestodal agent similar to praziquantel. The action of epsiprantel on parasites is related to neuromuscular toxicity and paralysis via altered permeability to calcium. Susceptible parasites include canine cestodes *Dipylidium caninum* and *Taenia pisiformis* and feline cestodes *D. caninum* and *T. taeniaeformis*.

## Indications and Clinical Uses

Like praziquantel, epsiprantel is used primarily to treat infections caused by tapeworms.

### Precautionary Information

#### Adverse Reactions and Side Effects

Vomiting occurs at high doses. Anorexia and transient diarrhea have been reported. Epsiprantel is safe in pregnant animals.

#### Contraindications and Precautions

Do not use in animals younger than 7 weeks. All doses are single dose.

#### Drug Interactions

No drug interactions are reported.

## Instructions for Use

Administer as directed to treat tapeworm infections.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Epsiprantel is available in 12.5-, 25-, 50-, and 100-mg coated tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 5.5 mg/kg PO.

### Cats

- 2.75 mg/kg PO.

## Large Animal Dosage

- No large animal doses are reported.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Ergocalciferol

er-go-kal-sif'eh-role

**Trade and other names:** Calciferol and Drisdol

**Functional classification:** Vitamin

## Pharmacology and Mechanism of Action

Vitamin D analogue. Vitamin D promotes absorption and utilization of calcium.

## Indications and Clinical Uses

Ergocalciferol is used for vitamin D deficiency and as treatment of hypocalcemia associated with hypoparathyroidism. Calcitriol often is used in place of ergocalciferol in dogs and cats. See calcitriol section for more information.

## Precautionary Information

### Adverse Reactions and Side Effects

Overdose may cause hypercalcemia.

### Contraindications and Precautions

Avoid use in pregnant animals because it may cause fetal abnormalities. Use cautiously with high doses of preparations containing calcium.

### Drug Interactions

No drug interactions are reported.

## Instructions for Use

Ergocalciferol should not be used for renal secondary hypoparathyroidism because of inability to convert to active compound. Doses for individual patients should be adjusted by monitoring serum calcium concentrations.

## Patient Monitoring and Laboratory Tests

Monitor serum calcium concentration.

## Formulations

- Ergocalciferol is available in 50,000 units per capsule.

### Conversion of Units

To convert: 1.0 units ergocalciferol is equivalent to 0.025 mcg ergocalciferol or cholecalciferol.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

- 500-2000 units/kg/day PO.

## Large Animal Dosage

- No large animal doses are reported.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Ertapenem

er-tah-pen'em

**Trade and other names:** Invanz

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Ertapenem is a beta-lactam antibiotic of the carbapenem (penem) class with a broad spectrum of activity. Its action on cell walls is similar to other beta-lactams, which is to bind penicillin-binding proteins (PBPs) that weaken or interfere with cell wall formation. In *Escherichia coli*, it has strong affinity toward PBPs 1a, 1b, 2, 3, 4, and 5, with preference for PBPs 2 and 3. Ertapenem is stable against hydrolysis by a variety of beta-lactamases, including penicillinases, and cephalosporinases and extended spectrum beta-lactamases. Spectrum includes gram-negative bacilli, including *Enterobacteriaceae*. Ertapenem is not as active against *Pseudomonas aeruginosa* as other carbapenems. It is also active against most gram-positive bacteria, except methicillin-resistant strains of *Staphylococcus* and *Enterococcus*. In people, the half-life is longer than other carbapenems (4 hours) because of high protein binding (95%), which allows for less frequent dosing. However, in dogs, these advantages do not exist. The protein binding in dogs is 46%, the volume of distribution is 0.28 L/kg, and the half-life is only 1.3 hours.

## Indications and Clinical Use

Ertapenem is indicated primarily for resistant infections caused by bacteria resistant to other drugs. It may be valuable for treating resistant infections caused by *E. coli* and *Klebsiella pneumoniae*. The use of ertapenem has not been as common as for meropenem or imipenem. High protein binding and long half-life in people have allowed less frequent administration compared to other carbapenems. However, dosing protocols have not been tested in dogs and cats.

## Precautionary Information

### Adverse Reactions and Side Effects

Carbapenems pose similar risks as other beta-lactam antibiotics, but adverse effects are rare. There is a risk of CNS toxicity (seizures and tremors) with high doses.

### Contraindications and Precautions

Some slight yellowish discoloration may occur after reconstitution. Slight discoloration will not affect potency. However, a darker amber or brown discoloration may indicate oxidation and loss of potency.

### Drug Interactions

Do not mix in vial or syringe with other antibiotics.

### Instructions for Use

Doses in animals have been based on extrapolation from human studies rather than efficacy trials.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are  $\leq 4$  mcg/mL for all organisms. Most bacteria have an MIC less than 2 mcg/mL. Sensitivity to imipenem can be used as a marker for ertapenem.

### Formulations

- Ertapenem is available in a 1-g vial for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 30 mg/kg qh8 (every 8 hours) IV or SQ.

### Large Animal Dosage

- No large animal doses have been reported.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Erythromycin

eh-rith-roe-mye'sin

**Trade and other names:** Gallimycin-100, Gallimycin-200, Erythro-100, and generic brands

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Macrolide antibiotic. Like other macrolides, it inhibits bacteria by binding of the 50S ribosome and inhibits bacteria protein synthesis. The spectrum of activity of erythromycin is limited primarily to gram-positive aerobic bacteria; it has little or no effect on gram-negative bacteria. The spectrum of activity also includes mycoplasma. In cattle, it is also active against respiratory pathogens such as *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni* (formerly *Haemophilus somnus*). Erythromycin effects on gastrointestinal (GI) motility are via stimulation of motilin receptors to increase smooth muscle activity. In dogs, the half-life is 1.3 hours IV and 2.9 hours oral, with only 11% bioavailability. In cats, the half-life is less than 1 hour.

In horses, the oral absorption is only 8%-26%, which contributes to diarrhea, and the half-life is short, necessitating frequent dose intervals.

### **Indications and Clinical Uses**

Erythromycin is used in a variety of species to treat infections caused by susceptible bacteria. Infections treated include respiratory infections (pneumonia), soft tissue infections caused by gram-positive bacteria, and skin and respiratory infections. In foals it is used to treat *Rhodococcus equi* pneumonia, often in combination with rifampin. In some species, including horses, it has been used at low doses to stimulate intestinal motility, but demonstration of this activity has been limited in clinical patients. In horses, the dose of erythromycin to stimulate GI motility is lower than the antibacterial dose (1 mg/kg), but the clinical efficacy for this use has not been shown. In experimental calves, 8.8 mg/kg IM significantly increased rumen motility. At a dose of 10 mg/kg IM in cows undergoing surgery for left displaced abomasum (LDA), it increased rumen contractions.

The use of erythromycin has diminished because of decreased availability of some dose forms (erythromycin estolate), adverse effects in small animals (vomiting), a short half-life that requires frequent dosing, and diarrhea in horses. Other macrolides have become used more often in each species. For example, azithromycin and clarithromycin are used in small animals and horses, and tilmicosin, gamithromycin, til-dipirosin, and tulathromycin are used more often in cattle instead of erythromycin.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Diarrhea in large animals is the most common adverse effect. This is believed to be caused by a disruption of the normal bacterial intestinal flora. This is caused usually from oral administration. Nursing mares have developed diarrhea through exposure to treated foals. Hyperthermia (febrile syndrome) in association with erythromycin treatment has been observed in foals.

In small animals, the most common side effect is vomiting (probably caused by cholinergiclike effect or motilin-induced motility). In small animals, it also may cause diarrhea. In rodents and rabbits, the diarrhea caused by erythromycin can be serious and even fatal.

#### **Contraindications and Precautions**

Do not administer orally to rodents or rabbits. Do not administer erythromycin solutions intended for IM administration by IV injection. Only the gluceptate and lactobionate salts should be used intravenously (gluceptate is rarely available).

#### **Drug Interactions**

Erythromycin, like other macrolides, is known to inhibit the cytochrome P450 enzymes and may decrease the metabolism of other coadministered drugs. See Appendixes H and I.

### **Instructions for Use**

There are several forms of erythromycin, including the ethylsuccinate and estolate esters and stearate salt for oral administration. However, the estolate form is only available as a suspension. There are no convincing data to suggest that one form is absorbed better than another, and the same dosage is included for all. Only erythromycin gluceptate and lactate are to be administered IV (gluceptate is rarely available). A motilinlike effect to stimulate GI motility occurs at low doses and has been studied primarily in experimental horses. Erythromycin may be administered to cattle in conjunction with surgical procedures to stimulate rumen motility postsurgery.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are  $\leq 0.25$  mcg/mL for streptococci and  $\leq 0.5$  for other organisms. Susceptibility to erythromycin tends to predict susceptibility to other macrolide antibiotics.

## Formulations

- Erythromycin is available in several forms that contain either a 250- or 500-mg erythromycin base. Oral formulations include 25- and 50-mg/mL erythromycin estolate suspension, 40-mg/mL erythromycin ethylsuccinate suspension, 400-mg ethylsuccinate tablets, and 250- and 500-mg erythromycin stearate tablets. Intravenous formulations include erythromycin lactobionate, but erythromycin gluceptate is rarely available. Erythromycin phosphate, a feed additive available as a powder, has been administered in horses and shown to produce adequate absorption. Erythromycin phosphate is 260 mg/g, which is equivalent to 231-mg erythromycin base per gram. This is available as an OTC feed additive for poultry.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Protect from freezing. Erythromycin base is most stable at pH 7-7.5. In acidic solution, it may decompose. Ethylsuccinate formulations are stable for 14 days.

## Small Animal Dosage

### Dogs and Cats

- 10-20 mg/kg q8-12h PO.
- Prokinetic effects (GI): 0.5-1 mg/kg q8-12h PO or IV.

## Large Animal Dosage

### Horses

- R. equi*: Erythromycin phosphate or erythromycin estolate 37.5 mg/kg q12h PO or 25 mg/kg q8h PO. Note that in horses, erythromycin base (plain tablets) are poorly absorbed and other forms should be used. (See instructions for dosing regarding dosage forms.)
- Erythromycin lactobionate injection: 5 mg/kg q4-6h IV. To stimulate GI motility: 1 mg/kg.

### Cattle

- Abscesses, pododermatitis: 2.2-8.8 mg/kg q24h IM.
- Pneumonia: 2.2-8.8 mg/kg q24h IM or 15 mg/kg q12h IM.
- Stimulate rumen motility: calves 8.8 mg/kg IM; cows 10 mg/kg IM.

## Regulatory Information

Cattle withdrawal times: 6 days meat (at 8.8 mg/kg). Do not use in female dairy cattle older than 20 months of age. Do not slaughter treated animals within 6 days of last treatment. To avoid excess trim, do not slaughter within 21 days of last injection. In Canada, withdrawal time for meat is 14 days and 72 hours for milk.

## Esmolol Hydrochloride

ez'moe-lole hye-droe-klor'ide

**Trade and other names:** Brevibloc

**Functional classification:** Beta blocker, antiarrhythmic

## **Pharmacology and Mechanism of Action**

Beta blocker. Selective for beta<sub>1</sub> receptor. The difference between esmolol and other beta blockers is the short duration of action is attributed to metabolism by red blood cell esterases; it has a half-life of only 9-10 minutes.

## **Indications and Clinical Uses**

Esmolol is indicated for short-term control of systemic hypertension and tachyarrhythmias. It has been used for emergency therapy or short-term treatment. Long-term treatment is not possible because of short half-life. Ordinarily, if an animal shows a positive response to esmolol, it can be switched to longer-acting beta blockers (e.g., propranolol or atenolol).

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects related to beta<sub>1</sub>-blocking effects on the heart include myocardial depression, reduced cardiac output, and bradycardia.

#### **Contraindications and Precautions**

When administering to patients with dilated cardiomyopathy, consider the risk of negative cardiac effects. Use cautiously in patients with bronchospasm. Esmolol is contraindicated in patients with bradycardia or atrioventricular (AV) block.

#### **Drug Interactions**

Use cautiously with digoxin, morphine, or warfarin.

## **Instructions for Use**

Esmolol is indicated for short-term IV therapy only. Doses are based primarily on empiricism or extrapolation of human dose. No clinical studies have been reported in animals.

## **Patient Monitoring and Laboratory Tests**

Monitor heart rate and rhythm during treatment.

## **Formulations**

- Esmolol is available in 10-mg/mL injection.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## **Small Animal Dosage**

### **Dogs and Cats**

- 0.5 mg/kg (500 mcg/kg) IV, which may be given as 0.05-0.1 mg/kg slowly every 5 min.
- CRI: 0.5 mg/kg slowly over a 30-60-second period followed by 50-200 mcg/kg/min infusion.

## **Large Animal Dosage**

### **Horses**

- 0.2 mg/kg over 1 minute IV. After 10 minutes, administer 0.5 mg/kg over 1 minute IV.
- CRI: 0.5 mg/kg IV, followed by 25 mcg/kg/min IV.

## Regulatory Information

Withdrawal times are not reported. However, because of short duration of action and rapid metabolism, a short withdrawal period is suggested.

RCI classification: 3

## Esomeprazole

Es-oh-mep'rah-zole

**Trade and other names:** Nexium

**Functional classification:** Antiulcer agent

## Pharmacology and Mechanism of Action

Proton pump inhibitor (PPI). Esomeprazole inhibits gastric acid secretion by inhibiting the  $K^+/H^+$  pump (potassium pump) located on the apical membrane of the gastric parietal cell, inhibiting secretion of  $H^+$  into the stomach. Like other PPIs, it produces a longer duration of acid suppression in a 24-hour period than other antiulcer drugs ( $H_2$  blockers). Other proton pump inhibitors include pantoprazole (Protonix), lansoprazole (Prevacid), omeprazole, and rabeprazole (Aciphex). They all act via similar mechanism and are equally effective. Proton pump inhibitors also have some effect for inhibiting *Helicobacter* organisms in the stomach when administered with antibiotics.

Omeprazole exists in two chiral isomers: the S- and R-isomer. The S-isomer is biologically active; thus esomeprazole represents the active form (S-isomer). In people, esomeprazole is metabolized more slowly, producing greater exposure, and has less variability. Otherwise, esomeprazole is almost identical to omeprazole in clinical effects.

## Indications and Clinical Uses

Esomeprazole, like other PPIs, is used for treatment and prevention of GI ulcers. It has not been used in dogs, cats, or horses as often as omeprazole, but would be expected to be equally effective if equipotent doses are administered. See the section on omeprazole for more detailed information.

Because of the long duration of effect, PPIs may be more effective than other drugs (e.g., histamine  $H_2$  blockers) for treating and inhibiting gastric ulcers.

Esomeprazole, like other PPIs, may be effective for preventing NSAID-induced ulcers than other antiulcer drugs.

## Precautionary Information

### Adverse Reactions and Side Effects

The use of esomeprazole has not been as common as with omeprazole. Therefore adverse effects have not been reported in animals with esomeprazole. However, consult the section on omeprazole for other information.

### Contraindications and Precautions

No contraindications have been reported for animals. There are concerns that long-term administration of PPIs in people can lead to *Clostridium*-associated diarrhea, risk of fractures, and hypomagnesemia. This has not been reported in animals. It is not known if long-term administration of PPIs to animals will lead to bacterial overgrowth in the stomach and intestine.



**Drug Interactions**

Although esomeprazole has not been associated with drug interactions in animals, PPIs may inhibit some drug-metabolizing enzymes (CYP450 enzymes). Because of stomach acid suppression, do not administer with drugs that depend on stomach acid for absorption (e.g., ketoconazole and itraconazole).

**Instructions for Use**

Omeprazole is the most common drug of this class used in animals, but esomeprazole would be expected to be equally effective if equipotent doses are administered. Other PPIs include pantoprazole (Protonix), lansoprazole (Prevacid), and rabeprazole (Aciphex). No experience with these other products is reported for veterinary medicine.

**Patient Monitoring and Laboratory Tests**

Esomeprazole and PPIs are generally considered safe. No routine tests for monitoring adverse effects are recommended. If gastrin concentrations are measured, a 7-day withdrawal from esomeprazole treatment should be used; otherwise, there is a significant increase in serum gastrin concentrations from esomeprazole treatment.

**Formulations**

- Esomeprazole is available in 20- and 40- mg delayed-release capsules; 2.5-, 5-, 10-, 20-, and 40-mg powder for delayed-release suspension; 20- and 40-mg esomeprazole sodium vials for injection; and 49.3-mg delayed-release capsules.

**Stability and Storage**

Esomeprazole should be maintained in the manufacturer's original formulation (capsules or suspension) for optimum stability and effectiveness. No information on stability of compounded formulations is available.

**Small Animal Dosage****Dogs**

- 20 mg/dog q24h PO or 1-2 mg/kg q24h PO; 1 mg/kg by IV injection.

**Cats**

- 1 mg/kg q24h PO.

**Large Animal Dosage****Horses**

- Treat ulcers: 4 mg/kg once daily for 4 weeks PO.
- Prevent ulcers: 1-2 mg/kg q24h PO.
- Treatment of ulcers: Loading dose of 1 mg/kg PO, followed by 0.5 mg/kg per day for 14-28 days.

**Regulatory Information**

Not intended for administration to animals that produce food. Oral absorption in ruminants is not established. Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI classification: 5

## Estradiol Cypionate

ess-trah-dye'ole sip'ee-oh-nate

**Trade and other names:** ECP, Depo-Estradiol, and generic brands

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Estradiol is used for estrogen replacement in animals. It also has been used to induce abortion in animals.

### Indications and Clinical Uses

Estradiol is a semisynthetic estrogen compound. Its effects will mimic that of estrogen in animals. The most common use in small animals has been to terminate pregnancy.

Estradiol benzoate also has been used to terminate pregnancy (5-10 mg/kg divided into two or three SQ injections). Estradiol cypionate formulation had high efficacy (95%), but it had serious adverse effects and is not recommended. Estradiol cypionate is longer acting and more potent than other estrogen formulations. Estradiol valerate injection (20 mg/mL) is also available for human medicine to treat hypogonadism.

### Precautionary Information

#### Adverse Reactions and Side Effects

Estradiol has a high risk of causing endometrial hyperplasia and pyometra. There is a dose-dependent risk of bone marrow toxicity in animals, particularly dogs. Estradiol cypionate injections have produced leukopenia, thrombocytopenia, and fatal aplastic anemia. Because stem cells can be affected, the bone marrow toxicity may not be reversible.

#### Contraindications and Precautions

Estradiol is contraindicated in pregnancy, unless used to terminate pregnancy. Do not administer to ferrets.

#### Drug Interactions

No drug interactions are reported for animals. It should not be used with other drugs that may suppress the bone marrow. In people, it has been recommended that these estrogen compounds not be used with other drugs that may cause hepatotoxicity. Estradiol may increase cyclosporine concentrations.

### Instructions for Use

To terminate pregnancy, 22 mcg/kg is administered once IM during days 3-5 of estrus or within 3 days of mating. However, in one study, a dose of 44 mcg/kg was more efficacious than a dose of 22 mcg/kg when given during estrus or diestrus.

### Patient Monitoring and Laboratory Tests

Monitor complete blood count (CBC) for evidence of bone marrow suppression.

### Formulations

- Estradiol is available in a 2-mg/mL injection. Estradiol valerate is available as 20 mg/mL injection in 5 mL vials.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- 22-44 mcg/kg IM (total dose not to exceed 1 mg).

**Cats**

- 250 mcg/cat IM, between 40 hrs and 5 days of mating.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

Do not use in food-producing animals.

**Estriol**

ess-tree-ole

**Trade and other names:** Incurin, Theelol (previously called Oestriol).

**Functional classification:** Hormone

**Pharmacology and Mechanism of Action**

Estriol is a natural estrogen hormone. It differs from DES or other estrogens because it is naturally occurring and occupies the receptor for a shorter duration compared to synthetic compounds (estradiol and DES). When used to treat urinary incontinence, its effects are believed to be caused by increasing sensitivity of alpha-adrenergic receptors in urinary smooth muscle.

**Indications and Clinical Uses**

Estriol is an estrogen replacement. In small animals, it has most often been used to treat urinary incontinence that is associated with estrogen deficiency, which is most common in dogs that have undergone ovariectomy.

**Precautionary Information****Adverse Reactions and Side Effects**

In field studies, the most common adverse effects were loss of appetite, vomiting, excessive water drinking, and swollen vulva. Estriol has not been associated with pyometra or bone marrow suppression compared to estradiol.

**Contraindications and Precautions**

Estriol is contraindicated in pregnancy. Do not administer to ferrets.

**Drug Interactions**

No drug interactions are reported for animals. It should not be used with other drugs that may suppress the bone marrow. In people, it has been recommended that these estrogen compounds not be used with other drugs that may cause hepatotoxicity, but such an interaction has not been shown in dogs.

**Instructions for Use**

To treat urinary incontinence, it has been used in combination with phenylpropanolamine (PPA); however, treatment addition of PPA may not improve efficacy compared to estrogen drugs used alone.

**Patient Monitoring and Laboratory Tests**

Monitor CBC for evidence of bone marrow suppression.

## Formulations

- Estriol is available as a 1-mg tablet.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 2 mg per dog PO q24h (may be combined with PPA). After starting with 2 mg per dog per day, after 1 week, reduce dose to 1.5 mg per dog per day for 1 week, then 1 mg per dog per day for 1 week, and a gradually tapered regimen and increased interval (every other day, every third day, etc.) until a goal of 0.5 mg per dog once per week is achieved.

### Cats

- No dose established.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Do not use in food-producing animals.

## Etidronate Disodium

eh-tih-droe'na-te dye-soe'dee-um

**Trade and other names:** Didronel

**Functional classification:** Antihypercalcemic agent

## Pharmacology and Mechanism of Action

Bisphosphonate drug. This group of drugs is characterized by a germinal bisphosphonate bond. They slow the formation and dissolution of hydroxyapatite crystals. Their clinical use resides in their ability to inhibit bone resorption. These drugs decrease bone turnover by inhibiting osteoclast activity and retard bone resorption and decrease the rate of osteoporosis. Other drugs in this class used in animals are alendronate, zoledronate (Zometa), pamidronate, clodronate (Osphos), and tiludronate (Tildren).

## Indications and Clinical Uses

The bisphosphonate group of drugs, which includes etidronate, is used primarily in people to treat osteoporosis and hypercalcemia of malignancy. In animals, they are used to decrease calcium in conditions that cause hypercalcemia, such as cancer and vitamin D toxicosis. Studies in people have shown that bisphosphonates may have action in cancer-induced bone disease that is more significant than the effect on osteolysis and bone resorption and also may decrease the tumor burden. In dogs, more experimental work has been performed with pamidronate than other drugs in this group. Some bisphosphonates have been used to treat navicular disease and bone spavin in horses. There are two bisphosphonates approved for treating horses, which are clodronate (Osphos), and tiludronate (Tildren).

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are not reported for animals, but use has been uncommon. In people, GI problems are common. Esophageal lesions have occurred because of reaction from contact with mucosa. If used in animals, ensure that tablets are completely swallowed.

### Contraindications and Precautions

No contraindications have been identified in animals.

### Drug Interactions

No drug interactions have been reported in animals. If mixed with other solutions or drugs, avoid mixtures containing calcium.

## Instructions for Use

At high doses, etidronate may inhibit mineralization of bone. In people, alendronate has replaced etidronate because of side effects. There are no clinical studies demonstrating efficacy of etidronate in animals; the use is extrapolated from human medicine and anecdotal experience.

## Patient Monitoring and Laboratory Tests

Monitor serum calcium and phosphorus. Monitor urea nitrogen, creatinine, urine-specific gravity in treated animals, and food intake.

## Formulations

- Etidronate is available in 200- and 400-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 5 mg/kg/day PO.

### Cats

- 10 mg/kg/day PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Withdrawal times are not established; 24-hour withdrawal times are suggested because this drug has little risk from residues.

## Etodolac

ee-toe'doe-lak

**Trade and other names:** EtoGesic (veterinary preparation) and Lodine (human preparation)

**Functional classification:** Nonsteroidal anti-inflammatory drug

## Pharmacology and Mechanism of Action

Like other NSAIDs, etodolac has analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclo-oxygenase enzyme (COX). The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a

healthy gastrointestinal (GI) tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is understood that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. In dogs, etodolac has a half-life of 7.6-14 hours, depending on the study and feeding conditions. In dogs, it shows either little preference for COX-2 or COX-1 (nonselective) or slight COX-2 selectivity in vitro. It is not known if selectivity for COX-2 affects efficacy or risk of adverse effects. In horses, etodolac is relatively COX-2 selective and is more potent than in dogs. The half-life in horses is only 3 hours, and a duration of effect of approximately 24 hours has been observed in horses with lameness.

### Indications and Clinical Uses

Etodolac is indicated for treatment of osteoarthritis in dogs. It also is used as an analgesic and may be used for other painful conditions. Like other NSAIDs, etodolac is expected to reduce fever. Uses in cats have not been established. Etodolac has been used in some horses to relieve pain associated with abdominal surgery and to treat lameness (e.g., caused by navicular disease). Dose regimens are different for horses compared with other animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Nonsteroidal anti-inflammatory drugs may cause GI ulceration. Other adverse effects caused by NSAIDs include decreased platelet function and kidney injury. In clinical trials with etodolac at recommended doses, some dogs showed weight loss, loose stools, or diarrhea. At high doses (above label dose), etodolac caused GI ulceration in dogs. Etodolac has been associated with keratoconjunctivitis sicca (KCS) in dogs, which in some cases has been severe. Resolution of KCS has occurred in only 10%-15% of cases after discontinuing medication. Improvement in KCS was greater if treatment duration was short. In horses, at high doses GI toxicity has been observed.

#### Contraindications and Precautions

Do not administer to animals prone to GI ulcers. Do not administer with other ulcerogenic drugs, such as corticosteroids. Do not administer to dogs that may be prone to developing KCS. Do not administer to animals with compromised renal function.

#### Drug Interactions

Use NSAIDs cautiously with other drugs known to cause GI injury (e.g., corticosteroids). The efficacy of ACE inhibitors and diuretics (furosemide) may be diminished when administered concurrently with NSAIDs. Etodolac may cross-react with sulfonamides in sensitive animals.

### Instructions for Use

Administer as directed and avoid concurrent use of other medications that may increase GI toxicity. Most of the use in dogs has been associated with treatment of osteoarthritis. In horses, it has been shown experimentally to improve lameness associated with navicular disease. When used in horses for this purpose, it was given at 23 mg/kg orally once or twice daily for 3 days. Treated horses improved with either regimen and showed no signs of adverse effects. Experimental horses treated with 20 or 23 mg/kg did not demonstrate adverse effects, but long-term safety has not been reported.

## Patient Monitoring and Laboratory Tests

Monitor for signs of GI ulcers and bleeding. Monitor tear production periodically in dogs treated with etodolac and observe for ocular signs of KCS. Monitor liver enzymes in dogs treated with NSAIDs periodically for signs of liver toxicosis. Monitor urea nitrogen and creatinine in treated animals for signs of kidney injury. Etodolac has had varying effects on  $T_4$ , free  $T_4$ , and thyroid-stimulating hormone (TSH) concentrations in dogs. One study showed no effect, and another study showed a decrease in  $T_4$  and free  $T_4$  in treated dogs after 2 weeks.

## Formulations

Etodolac is available in 150- and 300-mg tablets. Injectable 100 mg/mL. Human formulations include a 400-mg tablet, and 200-, and 300-mg capsules. Some formulations are no longer marketed in veterinary medicine.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Etodolac is insoluble in water, but is soluble in alcohol or propylene glycol.

## Small Animal Dosage

### Dogs

- 10-15 mg/kg once daily PO or 10-15 mg/kg injection SQ as a single dorsoscapular injection.

### Cats

- Dose not established.

## Large Animal Dosage

### Horses

- 23 mg/kg q24h PO. Long-term safety with this regimen has not been established (see instructions for dosing).

## Regulatory Information

No withdrawal times have been established. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI classification: 4

## Famciclovir

fam-sye'kloe-veer

**Trade and other names:** Famvir

**Functional classification:** Antiviral

### Pharmacology and Mechanism of Action

Antiviral drug. Famciclovir is a synthetic purine analogue (acyclic nucleoside analogue). It is converted to the antiviral drug penciclovir via di-deacetylation and oxidation. The conversion of famciclovir to penciclovir may be inefficient in cats, and oral absorption to the active drug is approximately 10% in cats, and can be variable. Penciclovir has antiviral activity against herpes virus type 1 (HSV1) and 2 (HSV2). The action is related to the affinity for the enzyme thymidine kinase (TK), which converts penciclovir into penciclovir triphosphate, which inhibits viral DNA polymerase to prevent DNA chain elongation—thus inhibiting viral DNA chain elongation. It is considered virostatic. It is used for treatment of various forms of herpes virus infection in humans and also has been used for treatment of viral infections in animals, particularly feline herpes virus 1 (FHV1). Feline herpes virus 1 is resistant to acyclovir and valacyclovir; therefore famciclovir (penciclovir) is the most promising oral drug to treat cats with FHV1 infection.

### Indications and Clinical Uses

The most common use of famciclovir in veterinary medicine is to treat FHV1 associated with conjunctivitis, rhinosinusitis, keratitis, and FHV1-associated dermatitis. Early studies with oral administration of famciclovir at 62.5 mg per cat failed to produce high enough blood concentrations of penciclovir to be consistently effective, but higher doses of 125 mg or more every 8-12 hours are now recommended based on clinical observations. In treated cats, there was improvement of conjunctivitis, decreased conjunctival inflammation, decreased ocular discomfort, and decreased tearing. When treating cats with conjunctivitis or upper respiratory disease, a tetracycline (minocycline or doxycycline) may be administered concurrently.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects observed from famciclovir in cats include mild anemia. Mild increase in white blood cells (WBCs) may be seen. No adverse effects were identified in limited studies performed in cats.

#### Contraindications and Precautions

Reduce dose in animals with compromised renal function. Safety in pregnant cats has not been studied.

#### Drug Interactions

No interactions identified.

### Instructions for Use

The dose listed for cats is based on limited studies in which 62.5 mg per cat was studied initially, but later evidence suggested that a higher dose of 125 mg per cat every 8-12 hours oral was more effective. Duration of treatment is undetermined, but generally 2 weeks may be needed.



## Patient Monitoring and Laboratory Tests

Monitor blood urea nitrogen (BUN) and creatinine during use.

## Formulations

- Famciclovir is available in 125-, 250-, and 500-mg tablets.

## Stability and Storage

Store tablets and capsules in tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Cats

- Treatment of feline herpes: 62.5 mg per cat PO q8h for 3 weeks. However, a higher dose of 125 mg per cat q8h may be more effective. Lower doses should be used in kittens (30-50 mg/kg oral q12h).

## Large Animal Dosage

### Horses

- No doses have been established.

## Regulatory Information

Because of mutagenicity, it should not be administered to animals intended for food.

## Famotidine

fah-moe'tih-deen

**Trade and other names:** Pepcid and generic

**Functional classification:** Antiulcer agent

## Pharmacology and Mechanism of Action

Histamine<sub>2</sub> antagonist (H<sub>2</sub> blocker). Stimulation of acid secretion in the stomach requires activation of histamine type 2 receptors (H<sub>2</sub> receptor), gastrin receptors, and muscarinic receptors. Famotidine and related H<sub>2</sub> blockers inhibit the action of histamine on the histamine H<sub>2</sub> receptor of parietal cells and inhibit gastric parietal cell gastric acid secretion. Famotidine increases stomach pH to help heal and prevent gastric and duodenal ulcers.

## Indications and Clinical Uses

Famotidine, like other H<sub>2</sub>-receptor blockers, is used to treat ulcers and gastritis in a variety of animals. Although it is often used for animals with vomiting, there are no efficacy data to indicate that it is effective. There are no efficacy data to support its use for preventing nonsteroidal anti-inflammatory drug (NSAID)-induced bleeding and ulcers. Famotidine has been used by veterinarians as a preferred H<sub>2</sub> blocker, but there is a lack of evidence to demonstrate superiority over other drugs in this class. Some studies have demonstrated efficacy at 1 mg/kg in dogs, while other studies have not demonstrated differences between famotidine and a placebo in dogs for increasing stomach pH.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects usually are seen only with decreased renal clearance. In people, central nervous system (CNS) signs may occur with high doses. The intravenous

(IV) solution contains benzyl alcohol, aspartic acid, and mannitol. Give IV injections slowly to cats (over 5 minutes) because rapid IV injections may cause hemolysis.

### Contraindications and Precautions

Intravenous solutions contain benzyl alcohol. Intravenous injections to small animals, especially cats, should be done slowly.

### Drug Interactions

Famotidine and other  $H_2$ -receptor blockers block secretion of stomach acid. Therefore they will interfere with oral absorption of drugs dependent on acidity, such as ketoconazole, itraconazole, and iron supplements. Unlike cimetidine, famotidine is not associated with inhibition of microsomal P450 enzymes.

### Instructions for Use

Administer with food for best absorption. Clinical studies for famotidine have not been performed; therefore optimal doses for ulcer prevention and healing are not known. Dose recommendations are extrapolated from human use or from anecdotal experience. Experimental studies in dogs have shown that doses of 0.1-0.2 mg/kg inhibit stomach acid secretion, but other clinical studies have shown that doses of 1.0 mg/kg suppress stomach acid for 24 hours. For IV use, dilute with IV solutions (e.g., 0.9% saline) to a total volume of 5-10 mL

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Famotidine is available in 20- and 40-mg tablets, 8-mg/mL oral suspension, and 10-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Famotidine is soluble in water. Compounded formulations in cherry syrup have been stable for 14 days. Diluted IV solutions in saline are stable for 48 hours at room temperature.

### Small Animal Dosage

#### Dogs

- 0.1-0.2 mg/kg q12h PO, IV, SQ, or IM. A dose of 40 mg/dog q12h has been used empirically. Doses as high as 0.5-1 mg/kg have been administered, but there is no evidence that higher doses will improve efficacy.

#### Cats

- 0.2 mg/kg q24h, up to 0.25 mg/kg q12h IM, SQ, PO, or IV (slowly over 5 minutes).

### Large Animal Dosage

#### Horses

- 1-2 mg/kg q6-8h PO.

### Regulatory Information

No restrictions on use in animals not intended for food.

Racing Commissioners International (RCI) classification: 5

## Febantel

feh-ban'tel

**Trade and other names:** Rintal and Vercom. Drontal Plus also contains two other drugs.

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Febantel is an antiparasitic that interferes with carbohydrate metabolism in parasitic worms. It suppresses mitochondrial reactions via inhibition of fumarate reductase and interferes with glucose transport. It is metabolized to a benzimidazole compound that binds to structural protein tubulin and prevents polymerization to microtubules, which results in incomplete digestion and absorption of nutrients by the parasite.

A formulation of febantel, pyrantel, and praziquantel (Drontal Plus) has been used in cats for treatment of *Giardia*, roundworms, hookworms, and whipworms.

### Indications and Clinical Uses

Febantel is indicated in the control and treatment of larvae and adult stages of intestinal nematodes. In horses, it is used for removal of large strongyles (*Strongylus vulgaris*, *S. edentatus*, *S. equinus*), ascarids (*Parascaris equorum*, sexually mature and immature), pinworms (*Oxyuris equi*, adult and fourth-stage larvae), and the various small strongyles.

In dogs and cats, it is used for treatment of hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*), ascarids (*Toxocara canis* and *Toxascaris leonina*), and whipworms (*Trichuris vulpis*). In dogs, it is used in combination with praziquantel for treatment of hookworms (*A. caninum* and *U. stenocephala*), whipworms (*T. vulpis*), ascarids (*T. canis* and *T. leonina*), and tapeworms (*Dipylidium caninum* and *Taenia pisiformis*).

In cats, it is used in combination with praziquantel for removal of hookworms (*A. tubaeforme*), ascarids (*Toxocara cati*), and tapeworms (*D. caninum* and *Taenia taeniaeformis*).

Febantel has been used with pyrantel (Drontal Plus) for treatment of *Giardia*.

### Precautionary Information

#### Adverse Reactions and Side Effects

Vomiting and diarrhea may occur after dosing.

#### Contraindications and Precautions

Do not use in pregnant animals. Do not use in animals with liver or kidney dysfunction.

#### Drug Interactions

No drug interactions reported.

### Instructions for Use

For horses, the paste may be administered on the base of the tongue or added to a portion of the normal grain ration. For most effective results, retreat in 6-8 weeks. Febantel suspension may be used in combination with trichlorfon oral liquid when combining 1 part febantel suspension with 5 parts trichlorfon liquid.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Febantel is available in an equine paste: 45.5% febantel (455 mg/mL), suspension: 9.3% febantel (2.75 g per ounce), and 27.2- and 163.3-mg tablets.
- Febantel is also available in combinations; each gram of paste contains 34 mg of febantel and 3.4 mg of praziquantel.
- Febantel, pyrantel, and praziquantel are available for small animals.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 10 mg/kg febantel alone or in combination with 1 mg/kg praziquantel PO with food once daily for 3 days.
- Puppies: 15 mg/kg febantel alone or in combination with 1.5 mg/kg praziquantel PO with food once daily for 3 days.
- For treatment of *Giardia*, it has been combined with pyrantel (27-35 mg/kg febantel + 27-35 mg/kg pyrantel) q24h PO for 3 days.

### Cats

- 10 mg/kg febantel alone or in combination with 1 mg/kg praziquantel PO in the food once daily for 3 days.
- Kittens: 15 mg/kg febantel alone or in combination with 1.5 mg/kg praziquantel.

## Large Animal Dosage

### Cattle

- 7.5 mL/100 kg body weight PO.

### Horses

- 6 mg/kg PO.

### Sheep and Goats

- 1 mL/20 kg body weight or 5 mL/25 kg PO.

## Regulatory Information

Not for use in horses intended for food. No other regulatory restrictions are listed.

## Felbamate

fel'bah-mate

**Trade and other names:** Felbatol and generic

**Functional classification:** Anticonvulsant

## Pharmacology and Mechanism of Action

Anticonvulsant. The action to treat seizures in animals may be via antagonism at the N-methyl-D-aspartate (NMDA) receptor and block effects of excitatory amino acids. The half-life in dogs is 5-6 hours, which may require frequent administration.

## Indications and Clinical Uses

Felbamate is used to treat epilepsy in dogs when they are refractory to other anticonvulsants. Other drugs are typically used first before attempting to add felbamate. It has been used in conjunction with other anticonvulsants. However, the use in animals has declined because of the availability of other drugs to treat refractory seizures, such as levetiracetam, zonisamide, gabapentin, and pregabalin.

## Precautionary information

### Adverse Reactions and Side Effects

In dogs, it has increased risk of liver injury. It also may cause tremors, salivation, restlessness, and agitation (usually at the high doses). Keratoconjunctivitis sicca (KCS) also has been reported in dogs. Some blood abnormalities, such as neutropenia lymphopenia and thrombocytopenia, have been reported. In people, the most severe reactions have been hepatotoxicity and aplastic anemia.

### Contraindications and Precautions

It may increase phenobarbital concentrations. It may be more likely to cause liver injury when used with phenobarbital.

### Drug Interactions

Possible interactions exist with drugs that either alter or are substrates for hepatic cytochrome P450 enzymes. (See Appendix.) It may increase phenobarbital concentrations if used concurrently.

## Instructions for Use

Dosing has been empirically in dogs. There are no controlled studies to document efficacy, but it is usually administered when animals have been refractory to other drugs, such as phenobarbital or bromide.

## Patient Monitoring and Laboratory Tests

Monitoring of plasma concentrations is helpful to assess therapy. Assays may be available in some commercial laboratories. Ideal plasma concentrations have not been established for animals. However, concentrations in humans of 24-137 mcg/mL in plasma have been effective (mean of 78 mcg/mL). Monitor complete blood count (CBC) and chemistry panels periodically (e.g., every 6 months).

## Formulations

- Felbamate is available in 120 mg/mL oral suspension, and 400- and 600-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- Start with 15-20 mg/kg q8h PO, and increase as needed to control seizures. Maximum dose is approximately 70 mg/kg q8h PO.
- Small dogs: 200 mg/dog q8h PO, and increase to a maximum dose of 600 mg/dog q8h.
- Large dogs: 400 mg/dog q8h. Increase dose gradually by 200-mg (15-mg/kg) increments until seizure control. Maximum dose for large dogs is 1200 mg/dog q8h.

### Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No withdrawal times have been established. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

RCI classification: 3

## Fenbendazole

fen-ben'dah-zole

**Trade and other names:** Panacur and Safe-Guard

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Benzimidazole antiparasitic drug. Like other benzimidazoles, fenbendazole produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in the parasite, eventually resulting in death. However, there is no effect on glucose metabolism in mammals.

### Indications and Clinical Uses

Fenbendazole is effective for treatment of numerous helminth intestinal parasites in animals, including *Toxacara*, *Toxascaris*, *Ancylostoma*, and *Trichuris*. In dogs, it is effective for most intestinal helminth parasites and also against nematodes. In dogs, it also has been used for pulmonary helminths (lungworms), but longer duration of treatment is needed. Fenbendazole has been effective for treatment of *Giardia*, but higher doses are needed and there may be failure rates as high as 50%. It is effective in cats for treatment of lungworms, flukes, and a variety of helminth parasites.

### Precautionary Information

#### Adverse Reactions and Side Effects

Fenbendazole has a good safety margin, but vomiting and diarrhea have been reported. When evaluated at doses of three and five times the recommended dose at three times the recommended duration, fenbendazole was well tolerated and no adverse effects were reported in the target species. It has been safe to use during pregnancy. There have been rare reports of pancytopenia associated with fenbendazole administration.

#### Contraindications and Precautions

No known contraindications. It may be used in all ages of animals.

#### Drug Interactions

There are no known drug interactions.

### Instructions for Use

Dose recommendations are based on clinical studies by the manufacturer. Granules may be mixed with food. Paste may be given to horses and cattle. Presence of food does not affect oral absorption. In studies for treatment of *Giardia*, it was safer than other treatments.

### Patient Monitoring and Laboratory Tests

Fecal monitoring may be performed to determine the efficacy of treatment for intestinal parasites.

### Formulations

- Fenbendazole is available in 22.2% (222 mg/g) Panacur granules, 10% oral paste (92 g/32 oz), and 100-mg/mL oral suspension.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 50 mg/kg/day for 3 days PO. Duration may be extended to 5 days for severe parasitic infestations. For pulmonary helminths (lungworms) in dogs, increase the duration of this dose to 10-14 days.

### Cats

- 50 mg/kg/day for 3 days PO.
- Duration may be extended to 5 days for severe parasitic infestations.

## Large Animal Dosage

### Horses

- Intestinal parasites, such as strongyles, pinworms, and ascarids: Panacur granules or paste is administered at a dose of 5.1 mg/kg (2.3 mg/pound) PO. Two packets of 1.15 g each will treat a 450-kg (1000-pound) horse. Panacur paste can be administered to horses at a dose of 5 mg/kg PO. Retreatment at 6-8 weeks may be necessary. For treatment of ascarids (*Parascaris equorum*) in horses, a higher dose of 10 mg/kg is recommended.

### Sheep and Goats

- 5 mg/kg PO.

### Cattle

- 5 mg/kg PO.

## Regulatory Information

Cattle withdrawal time (meat): 8 days. There is no withdrawal period for milk.

Goat withdrawal time: 6 days meat; 0 days milk.

## Fenoldopam mesylate

fe-nol'- doe- pam

**Trade and other names:** Corloпам

**Functional classification:** Vasodilator

## Pharmacology and Mechanism of Action

Fenoldopam is a dopamine agonist. It is specific for the dopamine D<sub>1</sub> receptors, without effects on alpha- or beta-adrenergic receptors, and therefore has been used to produce smooth muscle relaxation and vasodilation in vascular beds that have D<sub>1</sub> receptors (peripheral arteries and kidneys). It has no activity on D<sub>2</sub> receptors and only a small effect on alpha-adrenergic receptors. Because of this activity, fenoldopam has more specificity than dopamine, which has been used for similar indications. The use of fenoldopam is usually confined to increasing renal perfusion to treat acute renal failure. The half-life in animals is very short (1-7 minutes in dogs), with very high clearance (60 mL/min/kr), so it is usually administered via constant-rate infusion (CRI).

## Indications and Clinical Uses

The use of fenoldopam in veterinary medicine is limited to a few research studies (primarily in cats and dogs), clinical reports, and some anecdotal evidence of efficacy for treating acute kidney injury. It may act as a renal vasodilator, but there is insufficient evidence to recommend for routine treatment as there has been no demonstrated difference in survival associated with treatment. In people, it has replaced dopamine as a treatment of acute kidney injury. It is also used in people to treat severe hypertension, to prevent renal ischemia, to increase gastrointestinal (GI) perfusion, and to treat acute kidney injury. The use is limited to short-term in-hospital use when rapid treatment of hypertension is needed.

### Precautionary Information

#### Adverse Reactions and Side Effects

It has been generally safe and well-tolerated in dogs and cats. The most common side effect is hypotension. The half-life of fenoldopam is short; therefore if hypotension is observed, decrease the infusion rate. Other adverse effects described for small animals include reflex tachycardia and mild hypokalemia. Rarely it has caused facial twitching and hypersalivation in cats. In people, adverse effects can include increased intraocular pressure (risk in glaucoma), low potassium, and tachycardia.

#### Contraindications and Precautions

No known contraindications.

#### Drug Interactions

Use cautiously with other vasodilators; excessive hypotension can occur. Do not use with beta blockers.

## Instructions for Use

Administer by CRI. Do not administer bolus doses. Onset of effects should occur within 15 minutes of starting the CRI. Dose recommendations are based on some limited research studies and anecdotal clinical experience from veterinarians. There have been no well-controlled studies of efficacy in animals, and the use is largely extrapolated from human recommendations. It is recommended that the solution be added to fluids to make a 40-mcg/mL solution for infusion. For example, add 1 mL (10 mg) to 250 mL.

## Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and blood pressure during treatment.

## Formulations

- Fenoldopam is available as a 10-mg/mL injection. The pH range is 2.8-3.8.

## Stability and Storage

Fenoldopam solution can be mixed with sodium chloride solution (0.9%) or 5% dextrose solution for infusion. Once mixed in fluids, it is stable under normal ambient light and temperature conditions for at least 24 hours. After 24 hours, discard the solution.

## Small Animal Dosage

### Dogs

- 0.8 mcg/kg/min CRI.

### Cats

- 0.5-0.8 mcg/kg/min CRI.

## Large Animal Dosage

### Foals

- 0.04 mcg/kg/min.

## Regulatory Information

There are no withdrawal times established for food animals. Because fenoldopam has a very short half-life, residues in food animals are not expected to be a problem.



## Fentanyl Citrate (Note: Transdermal Fentanyl is Listed in Next Section)

fen'tah-nil sih'trate

**Trade and other names:** Sublimaze and generic brands; Fentora buccal tablets

**Functional classification:** Analgesic, opioid

### Pharmacology and Mechanism of Action

Synthetic opiate analgesic. Fentanyl is approximately 80-100 times more potent than morphine. Fentanyl is an agonist for the mu-opiate receptors on nerves and inhibits release of neurotransmitters involved with transmission of pain stimuli (such as substance P). The central sedative and euphoric effects are related to mu-receptor effects in the brain. Fentanyl has a wide safety profile with doses as high as 300 times the recommended dose not being lethal in spontaneously breathing dogs. It is highly lipophilic—approximately 1000 times more lipophilic than morphine, and low protein binding in dogs (15.6%), which produces rapid diffusion into the CNS. In dogs, the half-life is approximately 2-6 hours (depending on the study) and in cats, it is approximately 2.5 hours. Clearance is high, approximately equal to hepatic blood flow, and oral absorption is very low. Fentanyl can be absorbed from the skin or oral mucous membrane, but it is not orally bioavailable if swallowed.

### Indications and Clinical Uses

Fentanyl citrate is used as an IV bolus or as a CRI in animals for relief of pain, an adjunct for anesthesia, or as a sedative in combination with other CNS sedatives. Fentanyl administered by IV will produce antinociceptive effects for approximately 2 hours. Most of the doses are based on empiricism and experimental studies. Oral buccal tablets have been used in people for treatment of breakthrough pain, but there has been only anecdotal experience with this use in animals. See “[Fentanyl, Transdermal](#)” for information about the transdermal form. Clinical use is primarily in dogs and cats. In horses at doses needed to produce analgesia, it is associated with a high degree of restlessness, tachycardia, increased locomotor activity, and excitement (see “[Adverse Reactions and Side Effects](#)” section). In horses, there has been poor efficacy at lower doses.

### Precautionary Information

#### Adverse Reactions and Side Effects

Fentanyl has adverse effects similar to morphine. Like all opiates, side effects are predictable and unavoidable. Side effects include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses. As with other opiates, a slight decrease in heart rate is expected. In most cases, this decrease does not have to be treated with anticholinergic drugs (e.g., atropine), but it should be monitored. In horses, undesirable and even dangerous behavior can follow rapid IV opioid administration. Horses should receive a preanesthetic of acepromazine or an  $\alpha_2$ -agonist.

#### Contraindications and Precautions

Fentanyl citrate is a Schedule II controlled substance. Tolerance and dependence occur with repeated administration. Cats and horses are prone to excitement after administration, especially by IV.

#### Drug Interactions

There are no specific drug interactions, but fentanyl will decrease other anesthetic requirements. Fentanyl will potentiate other opiates and CNS depressants.

## Instructions for Use

Fentanyl injection is widely used in dogs and cats and some exotic species for management of pain and as an anesthetic adjunct. It is administered IV, via CRI, IM, and SQ. (Transdermal formulations are included in the next section.) For SQ administration, the pH of the solution (5.2) can elicit pain. The pain can be decreased by adding bicarbonate solution 1:10 and 1:20 dilution to increase pH to 8.0 for injection. In addition to fentanyl injection, transdermal fentanyl is available. Oral transmucosal (buccal) forms are available for human administration but have not been adequately tested in animals.

## Patient Monitoring and Laboratory Tests

Monitor analgesic response. Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

## Formulations

- Fentanyl citrate is available as a 250-mcg/5 mL injection (50 mcg/mL). Fentora buccal tablets are 100, 200, 400, 600, and 800 mcg.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water and slightly soluble in alcohol. It is a Schedule II drug, so store in a locked compartment. When compounded into a transmucosal gel, it has not been effective. The pH of fentanyl citrate is 5.2. If bicarbonate solution is added (1:10 or 1:20 dilution), the pH increases to 8.0, which may decrease pain from injection if injected immediately after mixing.

## Small Animal Dosage

### Dogs and Cats

- Anesthetic uses: 0.02-0.04 mg/kg q2h IV, SQ, or IM; if administered with acepromazine or diazepam, use 0.01 mg/kg IV, IM, or SQ.
- Analgesic agent, 0.005-0.01 mg/kg q2h IV, IM, or SQ.
- CRI for pain control in cats: Start with 3-5 mcg/kg (0.003-0.005 mg/kg) IV loading dose, then 2-5 mcg/kg/hr.
- CRI for pain control in dogs: Start with 0.003 mg/kg IV (3 mcg/kg) loading dose, followed by 0.005 mg/kg/hr (5 mcg/kg/hr) and increased to 10 mcg/kg/hr if necessary to control pain.

## Large Animal Dosage

### Small Ruminants

- 5-10 mcg/kg (0.005-0.010 mg/kg) IV.

## Regulatory Information

Schedule II controlled drug by Drug Enforcement Administration (DEA). No withdrawal information is available for food-producing animals.

RCI classification: 1

## Fentanyl, Transdermal

fen'tah-nil

**Trade and other names:** Duragesic (patches) and Recuvyra (transdermal solution)

**Functional classification:** Analgesic, opioid

### Pharmacology and Mechanism of Action

Synthetic opiate analgesic. Fentanyl is approximately 80-100 times more potent than morphine. Fentanyl is an agonist for the mu-opiate receptors on nerves and inhibits release of neurotransmitters involved with transmission of pain stimuli (such as substance P). The central sedative and euphoric effects are related to mu-receptor effects in the brain. Fentanyl transdermal has the same properties as fentanyl citrate administered by IV, except in this formulation it is administered transdermally to produce pain relief and as an adjunct to other drugs in perioperative patients and in patients with chronic pain. The fentanyl transdermal patch system delivers fentanyl through the skin at a constant rate to produce systemic effects. The fentanyl transdermal solution is rapidly absorbed in dogs to produce a peak concentration and maintains effective concentrations for treatment of pain for 4 days.

Fentanyl transdermal solution (50 mg/mL) is applied to the dorsal area of dogs and is absorbed systemically to produce sustained (4 days) duration of analgesia. The transdermal solution (Recuvyra) is approved for the control of postoperative pain associated with surgical procedures in dogs. This product is in an alcohol vehicle that dries rapidly on the skin, and the fentanyl penetrates to the skin to form a slowly releasing depot. A single dose (2.6 mg/kg; approximately 1 drop per kg) applied to the skin of dogs produces sustained blood concentrations. If applied prior to surgery, this product controls pain for at least 4 days.

Patches are available that deliver 25, 50, 75, and 100 mcg/hr. Absorption can be variable in animals (e.g., rate of release of fentanyl has varied from 27%-98% [mean 71%] of the theoretical value). Cats absorbed the fentanyl at an average rate of approximately one third that of the theoretical delivery rate, but one patch will maintain consistent concentrations of fentanyl in the plasma for at least 118 hours. Fentanyl transdermal patches (two or three 100-mcg/hr patches) have been applied to the skin of horses to relieve pain. In horses, the duration is less than in dogs or cats and may have to be reapplied every 48 hours.

### Indications and Clinical Uses

Transdermal fentanyl solution for dogs (Recuvyra) has been applied to dogs in field studies with proven efficacy in comparison to other opiate analgesics for perioperative pain. It has proven effectiveness for postoperative pain for a duration of up to 4 days after administration. Other than dogs, the use of the transdermal solution has not been evaluated in other animals.

Transdermal absorption from fentanyl patches has been demonstrated for cats, dogs, horses, and goats. In dogs, fentanyl transdermal patches (50 mcg/hr) are appropriate for most average-size dogs. Transdermal fentanyl has been shown effective to relieve postoperative pain in dogs. It has been well tolerated in cats. Fentanyl patches (25 mcg/hr) were effective and safe to relieve pain from onychectomy surgery in cats. Cats that have received fentanyl patches have had improvement in temperament, attitude, and appetite. Transdermal fentanyl has been used alone or combined with NSAIDs for treating severe pain in horses and may provide pain relief that is superior to NSAIDs alone.

## Precautionary Information

### Adverse Reactions and Side Effects

Severe adverse effects have not been reported. Typical opiate effects have been reported from the transdermal solution. The patch may cause slight skin irritation at the site of application. If patch delivery of fentanyl is high, some signs of opiate overdose may occur (e.g., excitement in cats or sedation in dogs); however, these reactions are rare. Adverse effects have not been reported from the use in horses. If adverse effects are observed in animals (e.g., respiratory depression, excess sedation, or excitement in cats), remove patch and, if necessary, administer naloxone hydrochloride (0.4-mg/mL solution at a dose of 0.04 mg/kg). If adverse effects are observed in dogs from fentanyl transdermal solution, administer naloxone at a dose of 0.4 mg/kg and repeat if necessary.

### Contraindications and Precautions

Transdermal fentanyl is a Schedule II controlled substance. Use cautiously in animals of small body weight (e.g., small toy dogs and young or debilitated cats). Consult the package insert and training guides supplied by the sponsor before administering transdermal fentanyl solution to dogs. Fentanyl has high potency and abuse potential in people. Animal owners should be advised of the high risks to humans if transdermal patches or transdermal solution is applied to humans. Fentanyl is absorbed through intact human skin.

### Drug Interactions

There are no specific drug interactions, but transdermal fentanyl will decrease other anesthetic requirements. Transdermal fentanyl will potentiate other opiates and CNS depressants.

## Instructions for Use

The fentanyl transdermal solution should be applied topically to the dorsal scapular area 2-4 hours prior to surgery. Use the provided syringe and applicator tips. Do not allow children, the pet owner, or other pets to contact the application area. Contact the manufacturer (sponsor) for training and instructions for application prior to clinical use. Initially apply up to ½ mL onto the skin without moving the applicator tip. If the calculated volume is greater than ½ mL, reposition the applicator tip at least 1 inch from the initial site and apply up to ½ mL. Repeat the reposition and application steps until the entire calculated volume has been applied to the dog. Restrain the dog for a full 2 minutes, and avoid contact with the application site for 5 minutes to allow complete drying of the solution.

Transdermal fentanyl incorporates fentanyl into adhesive patches applied to the skin of dogs and cats. Studies have determined that patches release sustained levels of fentanyl for 72-108 hours in dogs and cats. One 100-mcg/hr patch is equivalent to 10 mg/kg of morphine every 4 hours IM. Studies have determined that 25-mcg/hr patches are appropriate for cats. If rate of delivery is too high for cats and adverse reactions are suspected, covering half the adhesive surface area will reduce rate of delivery. A single 50-mcg/hr patch is appropriate for dogs weighing 10-20 kg. In horses, two or three 100-mcg/hr patches achieved rapid plasma concentrations within effective ranges in adults, but it was highly variable. Duration of effect in horses is less than in dogs or cats at only 48 hours. Follow manufacturer's recommendations carefully when applying patches.

**Patient Monitoring and Laboratory Tests**

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone. Monitor for signs of excitement in cats.

**Formulations**

- Fentanyl transdermal solution (Recuvyra) is supplied in 10-mL amber-colored glass vials (50 mg fentanyl/mL). Each vial is supplied with a purpose-designed needleless adaptor, syringes, and applicator tips.
- Transdermal fentanyl patches are available in 25-, 50-, 75-, and 100-mcg/hr patches. In May 2009 the formulation was switched to a matrix vehicle instead of a reservoir system. These have been bioequivalent to previous formulations in people.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Do not open the fentanyl patch membrane.

**Small Animal Dosage****Dogs**

- Patches: 10-20 kg: 50-mcg/hr patch q72h.
- Transdermal solution: 2.7 mg/kg (1.2 mg/pound) applied topically to the dorsal scapular area 2-4 hours prior to surgery.

**Cats**

- 25-mcg patch, per cat, q120h.
- Transdermal solution has not been evaluated for cats.

**Large Animal Dosage****Horses**

- Patches: In adult horses two or three transdermal patches of 100 mcg/hr each (10 mg fentanyl, equivalent to 35-110 mcg/kg delivered transdermally).
- Patches: In foals, one transdermal patch of 100 mcg/hr.

**Sheep and Goats**

- 100-mcg/hr patch. (Absorption has been inconsistent.)

**Regulatory Information**

Schedule II controlled drug by DEA.

Fentanyl should not be administered to animals that produce food. Withdrawal times are not established.

**Ferrous Sulfate**

fare'us sul'fate

**Trade and other names:** Ferospace and generic brands (over-the-counter [OTC])

**Functional classification:** Mineral supplement, iron supplement

**Pharmacology and Mechanism of Action**

Iron supplement. Replaces iron in animals that are deficient or with iron-deficiency anemia.

## Indications and Clinical Uses

Iron supplements are indicated in patients with diseases caused by iron deficiency.

### Precautionary Information

#### Adverse Reactions and Side Effects

High doses cause stomach ulceration. Feces become dark with oral administration.

#### Contraindications and Precautions

Do not use in animals prone to gastric ulcers. High doses or accidental ingestion may cause severe ulcers and perforation and should be treated as an emergency.

#### Drug Interactions

Iron supplements will interfere with oral absorption of other drugs such as fluoroquinolones, tetracyclines, and other drugs that may chelate with iron. Cimetidine and other antacids will decrease oral absorption because an acid environment favors absorption.

## Instructions for Use

Recommendations based on dose needed to increase hematocrit. In some animals, injectable iron dextran is used instead of oral therapy.

## Patient Monitoring and Laboratory Tests

Monitor hematocrit, serum iron levels, and total iron-binding capacity.

## Formulations

- Over-the-counter oral formulations are available; 250 mg ferrous sulfate contains 50 mg elemental iron. Injectable forms are usually iron dextran. (Iron dextran is listed in a separate monograph.)

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with other drugs because chelation may occur. Ferrous sulfate is soluble in water.

## Small Animal Dosage

### Dogs

- 100-300 mg/dog q24h PO.

### Cats

- 50-100 mg/cat q24h PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Extralabel withdrawal times are not established. However, 24-hour withdrawal times are suggested because this drug has little risk from residues.

## Finasteride

fin-ass'ter-ide

**Trade and other names:** Proscar

**Functional classification:** Hormone antagonist

## Pharmacology and Mechanism of Action

Finasteride is a synthetic steroid type-II 5 alpha reductase inhibitor. It inhibits conversion of testosterone to dihydrotestosterone (DHT). A similar drug in this class (but not evaluated in veterinary medicine) is dutasteride (Avodart).

## Indications and Clinical Uses

Because DHT stimulates prostate growth, finasteride has been used for benign prostatic hypertrophy (BPH). In dogs with BPH, finasteride has been shown to reduce prostatic size without adversely affecting testosterone production or semen quality.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse effects reported in dogs.

#### Contraindications and Precautions

Finasteride is contraindicated in pregnant animals.

#### Drug Interactions

No drug interactions are reported for animals.

## Instructions for Use

Doses are based on clinical studies in dogs, and information for other animals has not been reported. One study in dogs found significant effects at 0.1 mg/kg q24h. Another study used a dose range of 0.1-0.5 mg/kg q24h and reported reduction in prostate size.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Finasteride is available in 1- and 5-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

- 0.1 mg/kg q24h PO.
- Dogs 10-50 kg: 5-mg tablet per dog q24h PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No withdrawal times are established. Do not use in animals intended for food.

## Firocoxib

feer-oh-koks'ib

**Trade and other names:** Previcox and Equioxx

**Functional classification:** Anti-inflammatory

## Pharmacology and Mechanism of Action

Firocoxib is an NSAID. Like other drugs in this class, firocoxib produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by the NSAID is the cyclo-oxygenase (COX) enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is understood that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Firocoxib, using *in vitro* assays, is more COX-1 sparing compared to older NSAIDs and is a selective inhibitor of COX-2. The COX-1/COX-2 ratio is greater than for other drugs, indicating that firocoxib is a selective COX-2 inhibitor in dogs, horses, and cats. It has not been established if the specificity for COX-1 or COX-2 produces superior efficacy or safety compared to other less selective NSAIDs. Firocoxib has a half-life of 7.8 hours in dogs, 9-12 hours in cats, 11 hours in foals, 30-40 hours in adult horses, and 6.7 hours in calves. Because of shorter half-life, the concentrations are lower in foals compared to adult horses. It is highly protein bound (96%-98%). Oral absorption is 38% in dogs, 79%-100% in horses, approximately 100% in calves, and 54%-70% in cats. Feeding delays absorption but does not diminish overall absorption. In horses, oral absorption is 79%-100% with oral paste at a dose of 0.1 mg/kg, and 88% when the canine tablets are administered (no significant difference in absorption between oral paste and tablets). Fasted horses have higher absorption than fed horses.

## Indications and Clinical Uses

Firocoxib is used to decrease pain, inflammation, and fever. It has been used for the acute and chronic treatment of pain and inflammation in dogs. One of the most common uses is osteoarthritis, but it also has been used for pain associated with surgery. In horses, it is used for osteoarthritis. In cats, firocoxib has been demonstrated to be effective for attenuating acute febrile responses. Use in cats is limited to short-term use or long-term use at low doses.

## Precautionary Information

### Adverse Reactions and Side Effects

Gastrointestinal problems are the most common adverse events associated with NSAIDs and can include vomiting, diarrhea, nausea, ulcers, and erosions of the GI tract. Both acute and long-term safety and efficacy have been established for dogs prior to approval. In field trials, vomiting was the most often reported adverse effect. In studies performed in dogs, higher doses (five times the normal dose) caused GI problems. In horses, adverse effects have included oral ulcerations, renal papillary necrosis, and gastrointestinal effects after 42 days of dosing, but mucosal recovery after intestinal ischemia was less than other nonselective NSAIDs. In studies of young juvenile dogs, administration of firocoxib was associated with periportal fatty hepatic changes in some animals. Renal toxicity, especially in dehydrated animals or animals with preexisting kidney disease, has been observed for some NSAIDs. Behavior changes have occurred in dogs and horses, but they are rare.

In horses, GI problems (diarrhea, loose stool) have been reported in field trials, but they are rare at approved doses. At doses exceeding the labeled dose or duration in horses, ulcers, azotemia, renal injury, erosions of skin and oral mucosa, and prolonged bleeding times have been observed.



**Contraindications and Precautions**

Dogs and cats with preexisting GI problems or renal problems may be at a greater risk of adverse effects from NSAIDs. There is no information on the safety of firocoxib in the treatment of breeding, pregnant, or lactating animals, but adverse effects have not been reported in breeding animals.

In horses, do not exceed recommended duration of treatment. During animal safety studies in horses, toxicity occurred at recommended doses if administration exceeded 30 days.

**Drug Interactions**

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

**Instructions for Use**

Use according to manufacturer's dosing guidelines. Chewable tablets can be administered with or without food. Long-term studies have not been completed in cats, and only single-dose studies have been reported. The canine tablets have been administered orally to horses, with no significant differences in absorption compared to oral paste. Although this use is not allowed according to U.S. Food and Drug Administration (FDA) regulations, the oral tablets have been bioavailable in horses.

**Patient Monitoring and Laboratory Tests**

Monitor GI signs for evidence of diarrhea, GI bleeding, or ulcers. Because of risk of renal injury, monitor renal parameters (water consumption, BUN, creatinine, and urine-specific gravity) periodically during treatment.

**Formulations**

- Firocoxib is available in 57- and 227-mg tablets.
- Equine oral paste is available as 8.2 mg/g of paste (0.82% w/w).
- Equine injection is available as 20-mg/mL solution for IV use (with polyethylene glycol and glycerol vehicle).

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. It is not ionized and solubility is not affected by pH.

**Small Animal Dosage****Dogs**

- 5 mg/kg once daily PO.

**Cats**

- 1.5 mg/kg once, PO. Long-term safety in cats has not been determined.

**Large Animal Dosage****Horses**

- 0.1 mg/kg q24h PO for up to 14 days.
- Intravenous: 0.09 mg/kg IV once daily (2 mL per 1000 lbs, or 2.6 mL/1250 lbs; 1.5 mL/750 lbs).

**Calves**

- Dose not established, but 0.5 mg/kg PO or IV has been used q24h.

## Regulatory Information

Withdrawal time is not established for food animals, but 26 days for slaughter has been used for calves in other countries. Do not administer to horses that are used for human consumption.

In racing horses, it is not permitted to be used 12 hours prior to competition.

## Florfenicol

flore-fen'ih-kole

**Trade and other names:** Nuflor, Nuflor Gold, Resflor (flunixin and florfenicol) Aquaflor (fish formulation)

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Florfenicol is a thiamphenicol derivative with the same mechanism of action as chloramphenicol (inhibition of protein synthesis). However, it is more active than either chloramphenicol or thiamphenicol, and may be more bactericidal than previously thought against some pathogens (e.g., BRD pathogens). Florfenicol has a broad spectrum of antibacterial activity that includes all organisms sensitive to chloramphenicol, gram-negative bacilli, gram-positive cocci, and other atypical bacteria such as mycoplasma. Florfenicol is highly lipophilic, which provides high enough concentrations to treat intracellular pathogens and cross some anatomic barriers (penetration across the blood-brain barrier in cattle is 46%). The half-life of florfenicol is 2-3 hours in cattle after IV administration, but it is prolonged (18 hours) after IM injection, and 27 hours after 40 mg/kg subcutaneously. In dogs, the half-life is shorter, with values of 1.1 and 1.2 after IV and oral administration, respectively. The half-life in cats is approximately 4 hours and 7.8 hours after IV and oral administration, respectively.

## Indications and Clinical Uses

Because florfenicol is a derivative of chloramphenicol, it has been used in situations in which chloramphenicol is unavailable or illegal. (Chloramphenicol is illegal to use in food animals in the US.) Florfenicol has been shown to be effective for treatment of bovine respiratory disease (BRD) in cattle associated with *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni* (formerly *Haemophilus somnus*). Administration of florfenicol (40 mg/kg once SQ) at time of arrival to the feedlot decreased the incidence of BRD. It also is used for treatment of bovine interdigital phlegmon (foot rot, acute interdigital necrobacillosis, and infectious pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus* and for treatment of infectious bovine keratoconjunctivitis caused by *Moraxella bovis*. Resflor Gold contains both florfenicol and flunixin. It is used for the same BRD pathogens and provides anti-inflammatory activity with the addition of flunixin meglumine, including BRD-associated pyrexia in beef and nonlactating dairy cattle.

In pigs, it is used for treatment of swine respiratory disease (SRD) caused by *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Salmonella choleraesuis*, and *Streptococcus suis*. In cats, effective concentrations can be achieved with twice-daily administration. In dogs, the half-life is short, and frequent administration is necessary to produce effective concentrations. Florfenicol also has been administered to fish. There is a feed-additive formulation that also has been approved for catfish (10 mg/kg).

**Precautionary Information****Adverse Reactions and Side Effects**

Use in dogs and cats has been limited; therefore adverse effects have not been reported. Chloramphenicol has been linked to dose-dependent bone marrow depression, and similar reactions may be possible with florfenicol. However, there does not appear to be a risk of aplastic anemia as for chloramphenicol. At high doses, florfenicol may cause testicular degeneration. In horses, doses of 20 mg/kg q48h IM changed the bacterial flora and increased risk of diarrhea.

**Contraindications and Precautions**

Long-term use in animals may cause bone marrow suppression. Administration to horses has caused diarrhea, colitis, and elevations in bilirubin. Administration to horses is not recommended. Do not administer more than 10 mL in a single site.

**Drug Interactions**

No drug interactions are reported for animals. However, chloramphenicol is well known to inhibit cytochrome P450 enzymes and decrease metabolism of other drugs (see Appendix I). Therefore it is possible, but not documented, that florfenicol could cause drug interactions.

**Instructions for Use**

Dose form is only approved for use in cattle and pigs, and doses listed have not been thoroughly evaluated in small animals. Doses listed are derived from pharmacokinetic studies. Sustained effect in cattle from IM and SQ administration does not appear to be long lasting in dogs. Injectable formulation for cattle has been administered orally to small animals, if necessary, but the taste is bitter.

**Patient Monitoring and Laboratory Tests**

Monitor CBC for evidence of bone marrow depression. Susceptibility testing: laboratories have used chloramphenicol to test for susceptibility to florfenicol. Clinical and Laboratory Standards Institute (CLSI) break points for susceptible organisms are  $\leq 4$  mcg/mL for streptococci and  $\leq 8$  mcg/mL for other organisms.

**Formulations**

- Florfenicol is available in 300-mg/mL injectable solution (cattle) or 23-mg/mL solution to be added to drinking water for pigs (400 mg per gallon). Medicated feed formulation contains 500 g/kg to be added to fish feed. Flunixin is combined with florfenicol in Resflor Gold, which has 300 mg florfenicol and 16.5 mg flunixin per mL with vehicles of 2-pyrrolidone, 35 mg malic acid, and triacetin.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Light yellow or straw color does not affect potency. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- 20 mg/kg q6h IM or PO.

**Cats**

- 22 mg/kg q8h IM or PO.

**Large Animal Dosage****Cattle, BRD**

- 20 mg/kg q48h SQ or IM (in the neck).
- 40 mg/kg SQ as a single injection or q72h SQ in the neck region (also combined with flunixin at 2.2 mg/kg and Nuflor Gold at 40 mg/kg single injection).

**Horses**

- Although florfenicol has been administered, some references cite adverse effects after administration. Until more safety data become available, it is suggested to avoid use of florfenicol in horses.

**Pigs**

- 15 mg/kg IM in the neck q48h.
- Administer in drinking water at 400 mg per gallon (100 parts per million) for 5 consecutive days.

**Regulatory Information**

Cattle withdrawal time (meat): 28 days if administered IM; 38 days if administered SQ. Nuflor Gold withdrawal time (40 mg/kg SQ) is 44 days.

A withdrawal period has not been established in preruminating calves.

Do not use in calves to be processed for veal; not to be used in dairy cattle 20 months of age or older or in veal calves younger than 1 month.

Pig withdrawal time: 16 days after last treatment when administered in water; 13 days after last treatment when administered with feed.

**Fluconazole**

floo-kahn'ah-zole

**Trade and other names:** Diflucan and generic brands

**Functional classification:** Antifungal

**Pharmacology and Mechanism of Action**

Azole antifungal drug. Fungistatic. Fluconazole inhibits ergosterol synthesis in fungal cell membrane and has activity against dermatophytes, systemic fungi, and yeasts, including *Candida*, *Coccidioides*, and *Cryptococcus* spp. However, it has weak activity against molds such as *Aspergillus* or *Zygomycetes*. The two triazole rings on fluconazole make it less lipophilic and more water soluble than other azole antifungal agents. It is less protein bound than other azole antifungal drugs. Compared to other oral azole antifungals, fluconazole is absorbed more predictably and completely, even on an empty stomach. The half-life in dogs, cats, and horses is approximately 14-15, 13-25, and 38 hours, respectively.

**Indications and Clinical Uses**

Fluconazole is effective against dermatophytes, yeasts, and a variety of systemic fungi. In dogs, cats, horses, and exotic animals, it is used to treat systemic fungal infections, yeast infections, and dermatophytes, including *Malassezia* dermatitis. In cats, it has been used to treat *Cryptococcus* and histoplasmosis. In dogs, it is not as active against coccidioidomycosis as other azole antifungal drugs, but it has been effective in some patients. Higher doses may be needed (e.g., 10 mg/kg q12h) for coccidioidomycosis. It has been as effective as for treatment of blastomycosis in dogs with efficacy similar to itraconazole. Because it is water soluble, it has been used to treat fungal cystitis.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects have not been reported from fluconazole administration.

Compared to ketoconazole, it has less effect on endocrine function. However, increased liver enzyme concentrations and hepatopathy are possible.

**Contraindications and Precautions**

Use cautiously in pregnant animals. At high doses in laboratory animals, it has caused fetal abnormalities.

**Drug Interactions**

Fluconazole can be an inhibitor of cytochrome P450 enzymes, which can increase other drug concentrations. It will cause an increase in cyclosporine concentrations in dogs. It may decrease the metabolism of other drugs, such as anesthetics and sedatives (e.g., midazolam). Horses administered fluconazole had prolonged recovery from anesthesia, presumably caused by decreased anesthetic metabolism.

**Instructions for Use**

Doses for fluconazole are primarily based on studies performed in cats for treatment of cryptococcosis. Efficacy for other infections has not been reported. The primary difference between fluconazole and other azoles is that fluconazole attains higher concentrations in the CNS. Oral absorption of fluconazole is more predictable than itraconazole and ketoconazole and less affected by fasting.

**Patient Monitoring and Laboratory Tests**

Monitor hepatic enzymes periodically in treated animals. Susceptibility testing is possible, but ranges are only established for *Candida*. Fluconazole may cause mild elevations of liver enzymes in some dogs.

**Formulations**

- Fluconazole is available in 50-, 100-, 150-, and 200-mg tablets; 10- and 40-mg/mL oral suspension; and 2-mg/mL IV injection.

**Stability and Storage**

Fluconazole is stable for 14 days after reconstituting oral suspension. Because it is water soluble at a concentration of 8-10 mg/mL, it also may be compounded in formulations for administration to small animals. Tablets have been crushed and mixed with liquid vehicles for oral administration. However, long-term stability of compounded formulations beyond 15 days has not been determined.

**Small Animal Dosage****Dogs**

- 5 mg/kg q12h PO. In refractory cases, increase dose to 10 mg/kg q12h PO.
- Blastomycosis: 10 mg/kg per day.
- *Malassezia* treatment: 5 mg/kg q12h PO.

**Cats**

- 50 mg/cat per once daily PO; in refractory cases, increase to 50 mg per cat q12h PO (10 mg/kg q12h). In most cases it is administered once daily.

**Large Animal Dosage****Horses**

- 5 mg/kg q24h PO.

**Regulatory Information**

No withdrawal times are established for animals intended for food (extralabel use).

## Flucytosine

floo-sye'toe-seen

**Trade and other names:** Ancobon

**Functional classification:** Antifungal

### Pharmacology and Mechanism of Action

Antifungal drug. Action is to penetrate fungal cells and is converted to fluorouracil, which acts as antimetabolite.

### Indications and Clinical Uses

Flucytosine is an antifungal drug that has been limited in veterinary medicine to treat cryptococcal meningitis. It should be used in combination with amphotericin B (but not azole antifungal drugs) for treatment of cryptococcosis to improve efficacy and decrease resistance. The use is primarily confined to treatment of cryptococcosis in cats because it causes toxic reactions in dogs.

### Precautionary Information

#### Adverse Reactions and Side Effects

Anemia and thrombocytopenia are the most common adverse effects. Cutaneous and mucocutaneous eruptions have been observed with use of flucytosine in dogs.

#### Contraindications and Precautions

No specific contraindications have been identified for animals. Use in dogs is not recommended because of eruptions of skin reactions.

#### Drug Interactions

No drug interactions are reported for animals.

### Instructions for Use

Flucytosine is used primarily to treat cryptococcosis in animals. Efficacy is based on its ability to attain high concentrations in cerebrospinal fluid (CSF). Flucytosine may be synergistic with amphotericin B.

### Patient Monitoring and Laboratory Tests

Monitor CBC during treatment.

### Formulations Available

- Flucytosine is available in 250- and 500-mg capsules.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Compounded oral suspensions have been stable for 60 days.

### Small Animal Dosage

**Cats (not recommended for dogs)**

- 25-50 mg/kg q6-8h PO, up to a maximum dose of 100 mg/kg q12h PO.
- Cryptococcal meningitis: 20-40 mg/kg q6h PO.

### Large Animal Dosage

- No large animal doses have been reported.

### Regulatory Information

No withdrawal times are established for animals that are intended for food (extralabel use).

## Fludrocortisone Acetate

floo-droe-kor'tih-sone ass'ih-tate

**Trade and other names:** Florinef

**Functional classification:** Corticosteroid

### Pharmacology and Mechanism of Action

Mineralocorticoid replacement therapy. Fludrocortisone has high potency of mineralocorticoid activity compared to glucocorticoid activity. Fludrocortisone acts to mimic the action of aldosterone in the body, specifically to increase reabsorption of sodium in renal tubules.

### Indications and Clinical Uses

Fludrocortisone is used as replacement therapy in animals with adrenocortical insufficiency (Addison disease). It has high mineralocorticoid potency compared to the glucocorticoid potency. Desoxycorticosterone pivalate (DOCP) is used as an alternative in dogs when an intermittent injectable is desired rather than daily oral doses of fludrocortisone. In cats, fludrocortisone has been used to treat primary hyperaldosteronism.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are primarily related to glucocorticoid effects with high doses. Polyuria/polydipsia may occur in some animals. Long-term treatment for hypoadrenocorticism may result in glucocorticoid side effects. Administration of fludrocortisone causes a significant reduction in urine aldosterone.

#### Contraindications and Precautions

Although used as a mineralocorticoid, it may produce glucocorticoid side effects. Use cautiously in animals that may be at risk for corticosteroid side effects.

#### Drug Interactions

No drug interactions are reported for animals.

### Instructions for Use

Dose should be adjusted by monitoring patient response (i.e., monitoring electrolyte concentrations). In some patients, it is administered with a glucocorticoid and sodium supplementation (e.g., prednisolone/prednisone at a dose of 0.2-0.3 mg/kg/day). However, because it has retained some glucocorticosteroid activity, some animals may not require additional supplementation with glucocorticoids when receiving fludrocortisone.

### Patient Monitoring and Laboratory Tests

Monitor patient's electrolytes (especially sodium and potassium). Dose adjustment should be based on electrolyte monitoring to maintain these within a desired range. Fludrocortisone is used as a diagnostic test for primary hyperaldosteronism in cats. This suppression test can be performed as a confirmatory test in cats with basal urine aldosterone:creatinine ratio  $> 7.5 \times 10^{-9}$ ; suppression  $< 50\%$  indicates inappropriate aldosterone secretion. See [dosing](#) section for protocol.

### Formulations

- Fludrocortisone is available in 100-mcg (0.1-mg) tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is insoluble in water. When crushed tablets were prepared in various suspensions, they were stable for 14 days.

## Small Animal Dosage

### Dogs

- 15-30 mcg/kg/day (0.015-0.03 mg/kg) PO.

### Cats

- 0.1-0.2 mg/cat q24h PO. To test for primary aldosteronism, administer 0.05 mg/kg q12h, for 4 days, and measure effect with urine aldosterone-to-creatinine ratio. (The range is  $> 7.5 \times 10^{-9}$  in cats with hyperaldosteronism.)

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Extralabel withdrawal times are not established. However, 24-hour withdrawal times are suggested because this drug has little risk from residues.

RCI classification: 4

## Flumazenil

floo-may'zeh-nil

**Trade and other names:** Romazicon

**Functional classification:** Antidote

## Pharmacology and Mechanism of Action

Benzodiazepine receptor antagonist. Flumazenil blocks the action of benzodiazepines, such as diazepam, from the action on the gamma aminobutyric acid (GABA) receptor.

## Indications and Clinical Uses

Flumazenil has no therapeutic benefits of its own, but it is used as a reversal agent after benzodiazepine administration in people (not commonly used in veterinary medicine). Because of high first-pass effects, it cannot be administered orally; it must be injected.

## Precautionary Information

### Adverse Reactions and Side Effects

No adverse effects reported in animals.

### Contraindications and Precautions

Flumazenil may precipitate a seizure if used with tricyclic antidepressants (TCAs) or other drugs that can lower seizure threshold.

### Drug Interactions

Flumazenil may increase risk of seizures when used with other drugs known to inhibit the inhibitory neurotransmitter GABA.



### Instructions for Use

Flumazenil is used primarily to block effects of benzodiazepine drugs. It has been used to reverse overdoses of benzodiazepines (e.g., diazepam). Although it has been used experimentally for treating hepatic encephalopathy, its efficacy for this condition is not established.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Flumazenil is available in a 100-mcg/mL (0.1-mg/mL) injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 0.02 mg/kg (20 mcg/kg) IV.
- To reverse benzodiazepines: 0.2 mg (total dose), as needed, IV.

### Large Animal Dosage

#### Horses, Cattle, Swine, and Sheep

- To reverse benzodiazepines: 20 mcg/kg IV (0.02 mg/kg).

### Regulatory Information

Do not use in animals intended for food.

## Flumethasone

floo-meth'ah-sone

**Trade and other names:** Flucort, Fluosmin suspension, Anaprime suspension

**Functional classification:** Corticosteroid

### Pharmacology and Mechanism of Action

Potent glucocorticoid anti-inflammatory drug. Potency is listed by one reference as approximately 15 times that of cortisol and in veterinary references as 30 times that of cortisol and 6-7 times the potency of prednisolone. Anti-inflammatory effects are complex but primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. Use is for treatment of inflammatory and immune-mediated disease.

### Indications and Clinical Uses

Flumethasone, like other corticosteroids, is used to treat a variety of inflammatory and immune-mediated diseases. The dosing section contains the range of doses for replacement therapy, anti-inflammatory therapy, and immunosuppressive therapy. Flumethasone is used more often in large animals than small animals. Large-animal uses include treatment of inflammatory conditions, especially musculoskeletal disorders, and is used intra-articularly. In horses, flumethasone has been used for treatment of recurrent airway obstruction (RAO). In cattle, corticosteroids have been used in the treatment of ketosis.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic–pituitary–adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, and delayed wound healing and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and urinary tract infections (UTIs). In horses, additional adverse effects include risk of laminitis.

### Contraindications and Precautions

Use cautiously in patients prone to ulcers or infection and in animals in which wound healing is necessary. Use cautiously in animals with renal failure or diabetes and in pregnant animals. The manufacturer has warned that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

### Drug Interactions

Administration of corticosteroids with NSAIDs will increase the risk of GI injury.

## Instructions for Use

Doses are based on severity of underlying disease. For example, anti-inflammatory conditions require lower doses than immune-mediated conditions. For all conditions, cats often require higher doses than dogs. Note that the approved label dose for cattle and horses is in the range of 1.25–5 mg per animal or approximately 0.003–0.006 mg/kg (3–6 mcg/kg) for an adult animal. Considering that the potency of flumethasone may be similar to dexamethasone, many experts feel that the dose should be higher, in the range of 0.04–0.15 mg/kg. The manufacturer's label dose for dogs and cats is approximately 0.01–0.02 mg/kg per day, PO, IV, IM, or subcutaneously. But based on comparative potency, the manufacturer's dose may be low for some conditions.

## Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotrophic hormone (ACTH) stimulation test to monitor adrenal function.

## Formulations

Flumethasone is available in a 0.5-mg/mL solution for injection, 0.0625-mg tablets for small animal use; 2 mg/mL flumethasone acetate suspension for small animals, and 2-mg/mL liquid suspension for intra-articular use in horses.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- Anti-inflammatory uses: 0.15–0.3 mg/kg q12–24h PO, IV, IM, or SQ. **Note** that the manufacturer's label dose is 0.06–0.25 mg per dog per day, and 0.03–0.125 mg per cat per day (approximately 0.01–0.02 mg/kg), but this may be low based on relative potency.

## Large Animal Dosage

### Horses

- 1.25-2.5 mg per animal as a single dose IM or IV (approximately 0.003-0.006 mg/kg). This is the dose frequently listed on the product label. However, many experts prefer doses of 0.04-0.15 mg/kg as a single dose IV or IM.
- Intra-articular use in horses: 6-10 mg per joint of the 2 mg/mL suspension.

### Cattle

- 1.25-5 mg/animal as a single dose IV or IM. This is the dose frequently listed on the product label. However, many experts prefer doses of 0.04-0.15 mg/kg as a single dose IV or IM.

## Regulatory Information

There are no US withdrawal times established.

In Canada, cattle withdrawal time (meat): 4 days.

RCI classification: 4

## Flunixin Meglumine

floo-nix'in meg'loo-meen

**Trade and other names:** Banamine and generic brands

**Functional classification:** Nonsteroidal anti-inflammatory drug

## Pharmacology and Mechanism of Action

Flunixin is an NSAID. It and other NSAIDs produce analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the COX enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is understood that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Flunixin is not selective for either COX-1 or COX-2. Other anti-inflammatory effects may occur (such as effects on leukocytes), but have not been well characterized. In horses, the half-life is 2 hours, oral absorption of paste is 77%, and absorption of granules is 85%. However, access to hay will delay peak concentrations and oral absorption from granules and paste mixed with feed may be more erratic. In cattle, the half-life is 3-4 hours IV, and 6 hours in calves, but it is longer when administered IM. Oral absorption in cattle is 60%.

## Indications and Clinical Uses

Flunixin is used primarily for short-term treatment of moderate pain and inflammation. It has been used to treat abdominal pain in horses, to decrease signs of sepsis in horses, and to decrease clinical signs associated with coliform mastitis in cattle. In horses, as an adjunctive treatment for sepsis, it is used at a low dose of 0.25 mg/kg. The dose of 0.25 mg/kg is not an "antiendotoxin" dose, as is popularly characterized, as it does not directly inhibit endotoxin. But at this low dose it may inhibit prostaglandins responsible for hemodynamic effects during sepsis in horses. Flunixin has been used as a single dose for treatment of diarrhea in dairy calves. Flunixin at 2.2 mg/kg IV in cows with endotoxin mastitis did not affect milk production, but it decreased fever and improved rumen motility. Flunixin has been used as an adjunctive treatment, with antibiotics, for treatment of BRD in which it reduces

inflammatory lung reactions and reduces BRD-associated pyrexia. Resflor Gold contains both florfenicol and flunixin in the same formulation.

In pigs, flunixin is used for pyrexia associated with SRD.

In dogs and cats, flunixin has been used occasionally, but treatment is usually confined to one or two treatments because of risk of gastrointestinal toxicity (ulcers and perforation). Generally, other NSAIDs that have a better safety profile are used in dogs and cats.

## Precautionary Information

### Adverse Reactions and Side Effects

Most severe adverse effects are related to the GI system. Flunixin causes gastritis and GI ulceration with high doses or prolonged use. In horses, flunixin administration may affect recovery after ischemic injury to the intestine. Reduced renal perfusion has also been documented. Therapy in dogs should be limited to 4 consecutive days. In horses, if given IM it can result in myositis and abscess at the injection site.

### Contraindications and Precautions

Avoid use in pregnant animals near term. Do not use in calves to be processed for veal. Do not use in bulls intended for breeding because reproductive effects in this class of cattle have not been studied. Flunixin is approved for IV treatment in some food animals, but if the dose is administered IM or SQ, there is an increased risk of meat residues. Administration to cows with mastitis showed that elimination may be prolonged more than healthy cows, thus increasing the risk of violative residues, even when withdrawal times are followed. Do not use for treating heat stroke in animals.

### Drug Interactions

Ulcerogenic effects are potentiated when administered with corticosteroids. Coadministration with phenylbutazone will increase the risk of hypoproteinemia and gastric ulcers in horses. Flunixin, like other NSAIDs, may interfere with the action of diuretics such as furosemide and ACE inhibitors.

Coadministration with enrofloxacin in dogs increased flunixin plasma concentrations because of reduced clearance.

## Instructions for Use

Flunixin use in large animals is dependent on the condition treated. It may be administered oral, IM, or IV, but generally limit the treatment to once daily to avoid adverse effects on GI tract and kidney. It is not approved for small animals in the United States, but has been approved for use in small animals in Europe. It has been shown in experimental studies to be an effective prostaglandin synthesis inhibitor.

## Patient Monitoring and Laboratory Tests

Monitor for signs of GI bleeding and ulcers during treatment. Monitor serum albumin in horses because repeated administration of NSAIDs has caused hypoproteinemia in some horses.

## Formulations

- Flunixin is available in 250-mg packet granules in a 10-g packet and 10- and 50-mg/mL injection. It is also available as a paste, and each 30-g syringe contains flunixin meglumine equivalent to 1500 milligrams of flunixin. Flunixin is combined with florfenicol in Resflor Gold, which has 300 mg florfenicol and 16.5 mg flunixin per mL with vehicles of 2-pyrrolidone, 35 mg malic acid, and triacetin.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 1.1 mg/kg once IV, IM, or SQ.
- 1.1 mg/kg/day 3 day/week PO.
- Ophthalmic use (associated with ocular surgery): 0.5 mg/kg once IV.

## Large Animal Dosage

### Horses

- 1.1 mg/kg q24h for up to 5 days IV or IM. Note: In foals it has been shown that doses as low as 0.25 mg/kg inhibit prostaglandin synthesis during sepsis. Horses with colic are also often treated with low doses of 0.25 mg/kg IV q8h.
- Paste: 1.1 mg/kg q24h PO.
- Granules: 1.1 mg/kg/day PO (one packet per 500 pounds).

### Cattle

- 1.1-2.2 mg/kg (slowly) once a day for up to 3 days IV.
- In combination with florfenicol (Resflor Gold): 40 mg/kg florfenicol and 2.2 mg/kg flunixin administered SQ.

### Pigs

- 2.2 mg/kg, once IM.

## Regulatory Information

Cattle withdrawal time: 4 days for meat and 36 hours for milk. Risk of residues is higher if dose is administered IM or SQ, and the withdrawal time should be extended to at least 30 days for meat and 72 hours for milk if this route is used. If administered orally in cattle, the meat withdrawal time should be at least 8 days and the milk withdrawal time should be 48 hours.

Pig withdrawal time: 12 days.

RCI classification: 4

## Fluorouracil

floo-roe-yoo'rah-sil

**Trade and other names:** 5-fluorouracil, Aducril

**Functional classification:** Anticancer agent

## Pharmacology and Mechanism of Action

Anticancer agent. Antimetabolite. 5-fluorouracil (5-FU) is an analogue of thymidine and uracil, which are bases of DNA and RNA, respectively. When used as an anticancer agent, it disrupts DNA and RNA to inhibit cancer cell growth. Fluorouracil is used in veterinary anticancer protocols such as carcinomas, osteosarcoma, hemangiosarcoma, transmissible venereal tumor, and mast cell tumors.

## Indications and Clinical Uses

Fluorouracil is used in cancer protocols in dogs. It has been used as a component with other combination cancer regimens.

## Precautionary Information

### Adverse Reactions and Side Effects

The toxicity from fluorouracil is most evident in rapidly growing cells (bone marrow, intestinal epithelium, and epithelial cells). Fluorouracil causes mild leukopenia, thrombocytopenia, and CNS toxicity. In dogs, it has caused GI sloughing, vomiting, respiratory distress, myelosuppression, behavioral changes, seizures, other neurologic signs, and cardiac abnormalities.

Dogs have been accidentally exposed by consuming topical formulations intended for people. Doses of 40 mg/kg in dogs result in death, and doses of 20 mg/kg, 10 mg/kg, and 5 mg/kg have caused high, intermediate, and low toxic effects in dogs, respectively.

### Contraindications and Precautions

Do not use in cats.

### Drug Interactions

No drug interactions are reported for animals.

## Instructions for Use

Consult anticancer treatment protocol for precise dosage and regimen.

## Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow toxicity.

## Formulations

- Fluorouracil is available in a 50-mg/mL vial. It is also available in topical forms as 0.5%, 1%, 2%, and 5% solutions and 1% and 5% creams. The topical forms are used in people for skin tumors and keratosis.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 150 mg/m<sup>2</sup> once/week IV.

### Cats

- Do not use.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in food animals because it is an anticancer agent.

## Fluoxetine Hydrochloride

floo-oks'eh-teen hye-droe-klor'ide

**Trade and other names:** Prozac (human formulation); Reconile (veterinary formulation)

**Functional classification:** Behavior modification, selective serotonin reuptake inhibitor

## Pharmacology and Mechanism of Action

Antidepressant drug. Fluoxetine, like other drugs in this class, is classified as a selective serotonin reuptake inhibitor (SSRI). Its mechanism of action appears to be via

selective inhibition of serotonin reuptake and downregulation of 5-HT<sub>1</sub> receptors. Selective serotonin reuptake inhibitors are more selective for inhibiting serotonin reuptake than the TCA drugs. Fluoxetine is metabolized to norfluoxetine, which is an active metabolite. Oral absorption in dogs is 72% with a half-life of 6-10 hours. The metabolite norfluoxetine has a longer half-life of 48-57 hours. In cats, oral absorption is 100% with a half-life of 34-47 hours; the metabolite norfluoxetine has a half-life of 51-55 hours. Absorption in cats from transdermal administration is only 10%. Another SSRI used in animals is paroxetine (Paxil).

### **Indications and Clinical Uses**

Fluoxetine, like other SSRIs, is used to treat behavioral disorders such as separation anxiety, canine compulsive behaviors, and dominance aggression. In cats, it has been effective for decreasing urine spraying (1 mg/kg/day). In trials comparing fluoxetine with clomipramine for treating urine marking in cats, both drugs were equally effective for long-term use. However, the urine marking returned after discontinuation of the drug. In both dogs and cats, SSRIs have been used for pain syndromes, but there are no studies of efficacy published for this indication. In horses, fluoxetine has been used for “cribbing behavior” and other behavior disorders.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Fluoxetine has fewer adverse effects (especially antihistamine and antimuscarinic effects) compared to other antidepressant drugs. During clinical trials in dogs, adverse reactions included vomiting, decreased appetite, lethargy, depression, trembling, and shaking in some dogs; the most common were lethargy and decreased appetite. In rare cases, it may cause seizures. In dogs, at high doses of 10-20 mg/kg, it caused tremors, anorexia, aggressive behavior, nystagmus, emesis, and ataxia. Occasionally some of these signs may be seen at lower doses. In cats, nervousness or increased anxiousness has been observed. However, in trials used for treating urine spraying, few adverse effects were reported. In cats, 5 mg/kg produced tremors and 3 mg/kg produced anorexia and vomiting. However, cats have tolerated doses up to 50 mg/kg.

#### **Contraindications and Precautions**

Use cautiously in animals prone to aggression because it may decrease inhibition. In early pregnancy it appears to be safe but has caused pulmonary hypertension in experimental animals late in pregnancy.

#### **Drug Interactions**

Do not use with other behavior-modifying drugs such as other SSRIs or TCAs. Do not use with monoamine oxidase inhibitors (MAOIs). Administration with selegiline may induce a reaction. Because it is highly metabolized by the liver, it may be subject to interactions caused by cytochrome P450 inhibitors. (See Appendix I).

### **Instructions for Use**

Always use in conjunction with a comprehensive behavior modification protocol. Clinical efficacy of fluoxetine for separation anxiety in dogs has been established from clinical studies. Because of a long half-life, accumulation in plasma may take several days to weeks. There may be a delay in the onset of action of 2 weeks.

In some animals, paroxetine (Paxil) is preferred, which is available in tablets and has been used for smaller-size animals. Do not use transdermally; absorption is low.

### **Patient Monitoring and Laboratory Tests**

Use in animals has been relatively safe, and one should only monitor behavior changes.

## Formulations

- Fluoxetine is available in human formulations of 10-, 20-, and 40-mg capsules; 10-mg tablets; and 4-mg/mL oral solution. The veterinary formulations may no longer be available, but were in sizes of 8-, 16-, 32-, and 64-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water at 14 mg/mL and in alcohol at 100 mg/mL. Fluoxetine hydrochloride solution has been mixed with various juices and flavorings and found to be stable for 8 weeks. In one trial, it was mixed in tuna-flavored water for cats and retained effectiveness.

## Small Animal Dosage

### Dogs

- 1-2 mg/kg once daily PO.

### Cats

- 0.5-4 mg/cat q24h PO (0.5-1 mg/kg per day). Start with 1/4 tablet (2.5 mg) per cat, and increase as needed.
- Urine marking: 1 mg/kg q24h PO and increase to 1.5 mg/kg if there has been inadequate response.

## Large Animal Dosage

- Horses: 0.25-0.5 mg/kg PO once daily, mixed with grain.

## Regulatory Information

Do not administer to animals intended for food.  
RCI classification: 2

## Fluticasone Propionate

floo-tik'ah-sone proe-pee-oe-nayt

**Trade and other names:** Flovent

**Functional classification:** Corticosteroid

## Pharmacology and Mechanism of Action

Potent glucocorticoid anti-inflammatory drug with potency of 18 times that of dexamethasone. In patients with inflammatory airway diseases, glucocorticoids have potent anti-inflammatory effects on the bronchial mucosa. Glucocorticoids bind to receptors on cells and inhibit the transcription of genes for the production of mediators (cytokines, chemokines, adhesion molecules) involved in airway inflammation. A decrease in the synthesis of inflammatory mediators such as prostaglandins, leukotrienes, and platelet-activating factor caused by glucocorticoids also may be important. Glucocorticoids also play a role in enhancing the action of adrenergic agonists on beta-2 receptors in the bronchial smooth muscle, either by modifying the receptor or augmenting muscle relaxation after a receptor has been bound. Corticosteroids also may prevent downregulation of beta-2 receptors. Topical (inhaled) corticosteroids such as fluticasone or budesonide are used to avoid systemic effects. They typically have high first-pass effects and low systemic exposure if swallowed. Because of low systemic effects, fluticasone produces fewer systemic steroid effects than prednisolone, such as effects on water consumption, appetite, and systemic immunity.



## Indications and Clinical Uses

Fluticasone is used as an inhaled (topical) corticosteroid for treatment of airway disease. Most of the use has been established for cats, but it also could be used for dogs, horses, or other animals in which a special adapter can be used to deliver the drug via a metered-dose inhaler. In dogs and cats, the most common use is for inflammatory airway diseases such as asthma, bronchitis, or bronchospasm. For example, if a cat is given 2 puffs twice a day of a potent inhaled corticosteroid (e.g., budesonide, fluticasone) and allowed 5-7 breaths (10 sec) from a chamber (spacer), it may reduce the need for oral prednisolone in cats with feline asthma. When doses were compared in experimental cats, the low dose of 44 mcg twice daily was as effective as 110 or 220 mcg twice daily.

In horses, the most common use is for RAO, formerly called COPD.

## Precautionary Information

### Adverse Reactions and Side Effects

Although fluticasone systemic absorption is low, some systemic exposure will occur in animals. Side effects can occur, but are not expected to be as severe as with systemic corticosteroids. Adrenal suppression is expected to occur in treated animals (suppressed ACTH response) but may recover once treatment is discontinued.

### Contraindications and Precautions

Use cautiously in patients with oral or respiratory tract infections because immunosuppression may occur.

### Drug Interactions

Some systemic effects are possible but minimal. Administration of corticosteroids with NSAIDs will increase the risk of GI injury.

## Instructions for Use

The use is based on administration of fluticasone for treatment of airway diseases. It is delivered via a metered-dose inhaler. These inhalers can be used in animals if special adaptations, such as a spacer device, which are available for use in pediatrics or for cats, dogs, and horses, are used. When treating dogs and cats, doses listed in the dosing section can be used initially, then adjusted depending on response.

## Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform ACTH stimulation test to monitor adrenal function. Fluticasone, although minimally absorbed systemically, will suppress the ACTH response.

## Formulations

- Metered-dose inhaler at 44, 110, or 220 mcg per puff.

## Stability and Storage

Store in original container (metered-dose inhaler). Do not puncture container or attempt to remove drug from pressurized container. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- Start with 220 mcg per dose q12h delivered with metered-dose inhaler. As patient is stabilized, decrease dose gradually to 110 mcg per dose, and lower if possible.

**Cats**

- Start with 44 mcg per dose (one puff from a 44-mcg inhaler) twice daily. Increase the dose as needed to 110 mcg, then to 220 mcg.

**Large Animal Dosage****Horses**

- 1-2 mg per horse (6-12 puffs from 220-mcg inhaler) twice daily for airway disease.

**Regulatory Information**

There are no US withdrawal times established.

RCI classification: not established.

F

**Fomepizole**

foh-meh'pih-zole

**Trade and other names:** 4-Methylpyrazole, Antizol-Vet, and Antizol (human preparation)

**Functional classification:** Antidote

**Pharmacology and Mechanism of Action**

Fomepizole is an antidote for ethylene glycol (antifreeze) and methanol intoxication. It inhibits the dehydrogenase enzyme that converts ethylene glycol to toxic metabolites.

**Indications and Clinical Uses**

Fomepizole is used for treatment of acute ethylene glycol toxicosis in dogs and cats. In people, it is used for this purpose but also is registered for methanol poisoning. It should be used early for maximum success. Fomepizole was safe and effective in dogs in clinical trials if used within 8 hours of poisoning. In cats, it is effective if administered at high doses within 3 hours of ethylene glycol ingestion. When fommepezole is unavailable, ethanol can be used as an alternative.

**Precautionary Information****Adverse Reactions and Side Effects**

No adverse effects have been reported.

**Contraindications and Precautions**

Treatment should be initiated early for optimum effect. In cats, treatment should be initiated within 3 hours, using a dose that is higher than for dogs.

**Drug Interactions**

Fomepizole will inhibit the metabolism of other drugs and compounds that share a similar pathway as alcohol. Use cautiously with any other coadministered drugs.

**Instructions for Use**

The only use documented is for emergency management of ethylene glycol intoxication. Experimental studies have demonstrated effectiveness in dogs and cats (high doses in cats). In cats, administration of ethanol infusion is also effective. Administer 0.9% sodium chloride before administration of fomepizole. If used for treating methanol intoxication, include administration of folinic acid (Leucovorin) at a dose of 1 mg/kg.

**Patient Monitoring and Laboratory Tests**

Monitor renal function during treatment. Monitor urine output.

## Formulations

- **Note:** The veterinary-approved product has recently been withdrawn by the manufacturer. The human formulation, or ethanol, can be used as an alternative. Fomepizole is available in a 1-g/mL solution (Antizol), a human preparation. 1.5 g may be added to 30 mL saline solution for injection (50 mg/mL).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 20 mg/kg initially IV, then 15 mg/kg at 12- and 24-hour intervals, then 5 mg at 36 hours.

### Cats

- 125 mg/kg initially, followed by 31.3 mg/kg at 12, 24, and 36 hours after the initial dose. Continue doses every 12 hours until ethylene glycol is no longer detected. If analysis of ethylene glycol is not available, treat with 31 mg/kg every 12 hours through 60 hours.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No withdrawal times are established for animals intended for food. There is little risk of residues in food animals.

## Fosfomycin Tromethamine

fos-foe-mye'-sin troe-meth'-ah-meen

**Trade and other names:** Monurol

**Functional classification:** Antibacterial (urinary)

## Pharmacology and Mechanism of Action

Fosfomycin is a urinary antimicrobial. It inhibits cell walls of susceptible bacteria and may decrease virulence by inhibiting the adherence of bacteria to bladder mucosa. It produces adequate concentrations in urine to manage UTIs. The concentrations in other tissues may not be high enough for treatment of non-UTIs. In people, it is used as a single dose to treat an acute UTI. In dogs, the half-life is short (1.1 hours IV and 2-3 hours oral), with good oral absorption. For gram-negative urinary pathogens, the mutation frequency for resistance is high. This raises concerns related to the potential for the development of resistance to fosfomycin during therapy.

## Indications and Clinical Uses

Fosfomycin is used as treatment or adjunctive treatment for UTIs. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. In women, it is used as a single dose to treat acute UTIs.

## Precautionary Information

### Adverse Reactions and Side Effects

No adverse effects have been reported. It has been safe and well tolerated in dogs up to 120-200 mg/kg.

### Contraindications and Precautions

Do not administer in dry form; mix with water. There are no other known contraindications. Fosfomycin should not be substituted for antibiotics with established efficacy.

### Drug Interactions

No known drug interactions.

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## Instructions for Use

Fosfomycin has been used to treat UTIs in animals, primarily when other drugs have failed or were inactive as a result of resistance. Alternatively, fosfomycin has been used intermittently (pulse therapy) to prevent recurrences of UTIs. The efficacy of any of these indications is not established in animals.

## Patient Monitoring and Laboratory Tests

Monitor UTI with culture and urinalysis.

## Formulations

- Fosfomycin is available in a 3-g packet. The packet also contains saccharin and sucrose for flavoring. This packet may be mixed with water and administered immediately orally.

## Stability and Storage

Store in original package, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs:

- Precise doses are not established for dogs. 75-150 mg/kg q12h PO has been recommended based on pharmacokinetic studies. Additional cited doses used are empiric and include a recommendation of a 3-g packet divided equally into three daily doses (1 g dissolved in 30 mL) and administered daily to dogs.

### Cats:

- No doses have been established for cats.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No withdrawal times are established for animals intended for food.

## Furazolidone

fyoo-rah-zole'ih-done

**Trade and other names:** Furoxone

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Furazolidone is an oral antiprotozoal drug with activity against *Giardia*, and it may have some activity against bacteria in the intestine. It is used for only local treatment of intestinal parasites; it is not used for systemic therapy.

## Indications and Clinical Uses

Furazolidone has been used to treat protozoal intestinal parasites. However, because efficacy and safety of other oral antiprotozoal drugs are better established, they are used more often.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are not reported in animals. In people, mild anemia, hypersensitivity, and disturbance of intestinal flora have been reported.

#### Contraindications and Precautions

No contraindications reported for animals.

#### Drug Interactions

Do not use with MAOIs.

## Instructions for Use

Clinical studies have not been reported for animals. Doses and recommendations are based on extrapolation from humans. Other drugs, such as fenbendazole, may be preferred for treating *Giardia*.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Furazolidone has been discontinued in the US. It may be available through some compounding pharmacies. Previously available tablet was 100 mg.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

- 4 mg/kg q12h for 7-10 days PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Furosemide

fyoo-roe'seh-mide

**Trade and other names:** Lasix and generic brands

**Functional classification:** Diuretic

## Pharmacology and Mechanism of Action

Furosemide is a loop diuretic that inhibits the  $\text{Na}^+/\text{K}^+/\text{2Cl}^-$  cotransporter in the ascending thick loop of Henle. It is often called a *high-ceiling diuretic* because it is more effective than other diuretics. Furosemide decreases the sodium, chloride, and potassium reabsorption from the tubule. Subsequently, these ions are retained in the renal tubule and presented to the distal nephron. Dilute urine is produced because water is retained in the tubule when it reaches the distal tubule. In addition, there is an associated urine loss of  $\text{Mg}^{++}$  and  $\text{Ca}^{++}$ . An additional mechanism of action is via prostaglandin synthesis. Furosemide increases intrarenal prostaglandin production (e.g.,  $\text{PGI}_2$ ), which increases renal blood flow. Synthesis of prostaglandins also may cause vasodilation in other tissues. The plasma half-life in animals is short (1.5-3 hours); therefore this is a short-acting drug, with a maximum onset of effect of 1-2 hours, and duration of 2-4 hours. Oral absorption can be highly variable, but in dogs is as high as 77%. Subcutaneous absorption is as high as other injectable routes. In horses, oral absorption is so low that this is not a viable method of administration.

## Indications and Clinical Uses

In small animals, furosemide is the drug of choice to treat conditions that cause edema: pulmonary edema, liver disease, heart disease, and vascular disease. Furosemide will increase  $\text{K}^+$  and  $\text{Ca}^{++}$  excretion and is used to treat hyperkalemia and hypercalcemia. The use of furosemide for acute kidney injury treatment has no benefit based on available evidence. Furosemide has no significant effect on patient outcomes when used for acute kidney disease. In horses, it has been used to treat edema and syndromes associated with congestion. The most common use in horses is pretreatment prior to racing. Although it appears to produce faster racing times, the mechanism is unclear. It may decrease body weight via water loss and may decrease exercise-induced pulmonary hemorrhage (EIPH). However, the efficacy to reduce EIPH has been controversial in horses. In cattle, furosemide also is used for treating conditions of edema (e.g., udder edema) and for treatment of heart failure and pulmonary hypertension.

In all animals, duration of effect is short, approximately 2-4 hours. Because of short duration, constant rate infusions (CRI) can produce greater efficacy in some animals.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are primarily related to diuretic effect (loss of fluid and electrolytes). In dogs, hyponatremia is more common than hypokalemia. Tolerance and activation of the renin-angiotensin-aldosterone system (RAAS) occur with repeated administration, in which the diuretic effect is attenuated. When administered to dogs at a dose of 2 mg/kg q12h, it significantly increased RAAS activity by day 5 of treatment. When the RAAS is activated, increased concentrations of aldosterone can have persistent and deleterious effects on vasculature and cardiac remodeling. As subcutaneous injection may cause irritation (stinging) at the injection site.

### Contraindications and Precautions

Administer conservatively in animals receiving ACE inhibitors to decrease the risk of azotemia. Repeated administration may increase aldosterone levels via activation of RAAS.

### Drug Interactions

Concurrent use with aminoglycoside antibiotics or amphotericin B may increase risk of nephrotoxicity and ototoxicity. Administration of NSAIDs with furosemide may diminish the effect. The pH of solution is 8-9.8. Furosemide is stable with alkaline drugs, but do not mix with acidifying drug solutions with pH <5.5.

## Instructions for Use

Recommendations are based on extensive clinical use of furosemide in animals. The onset of effect after an injection is usually 5 minutes, with the peak at 30 minutes to 2 hours and a duration of approximately 2 to 4 hours. Constant-rate infusions in dogs and horses can be more effective than intermittent bolus. Long-term repeated administration may attenuate the effects because of tolerance and activation of the RAAS.

## Patient Monitoring and Laboratory Tests

Monitor electrolyte concentrations (particularly potassium) and hydration status in patients during treatment.

## Formulations

- Furosemide is available in 12.5-, 20-, 40-, 50-, and 80-mg tablets; 20-, 40-, and 80-mg tablets (human preparation); 10-mg/mL oral solution (syrup), and 50-mg/mL injection. Tablets usually can be easily split. A 2 gram bolus is available for large animals, but oral absorption is uncertain.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with acidic solutions. It is compatible in plastic syringes and infusion sets. Furosemide is poorly soluble in water, but may be mixed with 5% dextrose, 0.9% saline, or lactated Ringer's solution at a concentration of 10 mg/mL. These solutions are stable for 8 hours. It is more soluble if the pH is  $>8$ , but it readily precipitates when pH is  $<5.5$ . Compounded oral formulations in syrups and other flavorings are stable if kept at alkaline pH or in alcohol. However, lower pH will result in instability of formulation. If discoloration occurs, discard formulation.

## Small Animal Dosage

### Dogs

- 2-6 mg/kg q8-12h (or as needed) IV, IM, SQ, or PO. A common initial dose when treating heart failure patients is 2 mg/kg q12h PO, then lower to 1-2 mg/kg q12h, PO.
- In acute cases where intensive treatment is needed, administer 2 mg/kg IV, followed by 2 mg/kg every 30 minutes, until improvement is seen.
- CRI: 0.66 mg/kg bolus dose IV, followed by 0.66 mg/kg/hr for 8 hours. Alternatively, a dose of 2 mg/kg in 5% glucose can be infused over an 8 hour period IV.

### Cats

- Start with 1 mg/kg, then increase as needed, within a range of 1-4 mg/kg q8-24h IV, IM, SQ, or PO.

## Large Animal Dosage

### Horses

- 1 mg/kg q8h or 250-500 mg/horse at 6-8 hour intervals IM or IV.
- CRI: 0.12 mg/kg IV followed by 0.12 mg/kg/hr IV.

### Cattle

- 500 mg/animal once a day or 250 mg/animal twice a day IM or IV.

## Regulatory Information

Cattle withdrawal times: 2 days meat and 48 hours milk.

Horses: Most racing regulations specify that a 250-mg/horse dose may be given by a single IV injection no later than 4 hours before racing post time. In most horses, this will not produce violations above 100 ng/mL urine threshold at 4 hours.

## Gabapentin

gab'ah-pen-tin

**Trade and other names:** Neurontin and generic brands

**Functional classification:** Anticonvulsant, analgesic

### Pharmacology and Mechanism of Action

Anticonvulsant and analgesic. Gabapentin is an analogue of the inhibitory neurotransmitter gamma aminobutyric acid (GABA); however, it is not an agonist or antagonist for the GABA receptor. The mechanism of anticonvulsant action and analgesic effects is not clear, but there is evidence that the mechanism of action appears to be via blocking calcium-dependent channels. Gabapentin inhibits the alpha-2-delta ( $\alpha_2 \delta$ ) subunit of the N-type voltage-dependent calcium channel on neurons. Through inhibition of these channels, it reduces the calcium influx that is needed for release of neurotransmitters—specifically, excitatory amino acids—from presynaptic neurons. Blocking the channels has little effect on normal neurons, but it may suppress stimulated neurons involved in seizure activity and pain. Half-life in dogs and cats is only 3-4 hours (2.8 hours in cats), which may necessitate frequent administration. In horses, the half-life is 8 hours (range 6.7-12 hrs), or 3-4 hours, depending on the study, but the oral absorption is only 16% resulting in lower plasma concentrations in horses compared to other animals. Another related drug is pregabalin (Lyrica), which is used in people for neuropathic pain and has also been used in dogs. Gabapentin is eliminated entirely by renal clearance in people, but there is 30%-40% hepatic metabolism in dogs. Therefore, drugs that affect liver metabolism, or severe liver disease may decrease gabapentin clearance in dogs.

### Indications and Clinical Uses

Gabapentin is used as an anticonvulsant, sedative, anxiolytic, and to treat chronic pain syndromes, including neuropathic pain. It is used to treat neuropathic pain that does not respond to nonsteroidal anti-inflammatory drugs (NSAIDs) or opiates. However, studies demonstrating efficacy for pain treatment in dogs and cats are currently lacking. It was not effective for postoperative pain in dogs, and was not effective in a thermal nociceptive study in experimental cats at doses up to 30 mg/kg. In horses, it has been used to treat laminitis and other pain syndromes, but efficacy has not been shown in well-controlled studies. In calves, it has a long half-life, but was not effective for analgesia in dehorning procedures.

When used to treat epilepsy, it (or pregabalin) is usually considered when the seizures have become refractory to other drugs. Neurologists consider gabapentin an “add-on” for treating seizures in animals, but it is not very effective when used alone. When included in a regimen as an add-on, it is not as effective as zonisamide or levetiracetam.

### Precautionary Information

#### Adverse Reactions and Side Effects

Sedation and ataxia are reported adverse effects. As dose increases in dogs (see dosing section), sedation is more likely. In people, a withdrawal syndrome from abrupt discontinuation has been described, but it is not reported in animals. The oral solution contains xylitol, which is an artificial sweetener that can be toxic to dogs and produces hypoglycemia and liver injury with high doses exceeding 0.1 g/kg. With standard doses of gabapentin oral solution, the toxic level of xylitol is not likely to be exceeded, but one should be cautious about adding other drugs that also contain xylitol.



**Contraindications and Precautions**

No known contraindications.

**Drug Interactions**

Antacids decrease oral absorption.

**Instructions for Use**

Gabapentin has been used in some animals as an anticonvulsant when they are refractory to other drugs. It can be used with other drugs such as phenobarbital and bromide. It also has been used to treat neuropathic pain syndromes and can be used with NSAIDs and opioids. Efficacy for each of these indications is anecdotal; there are no controlled studies published to show efficacy for treating pain syndromes in animals.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary. If plasma/serum drug concentrations are monitored, the targeted trough concentration is 2 mcg/mL in dogs.

**Formulations**

- Gabapentin is available in 100-, 300-, and 400-mg capsules; 100-, 300-, 400-, 600-, and 800-mg scored tablets; and 50-mg/mL oral solution. A gastroretentive tablet is available (Gralise) that releases for 10 hours in people and is used once daily, but has not been evaluated in dogs or cats.

**Stability and Storage**

If stored at high temperatures and high humidity, there may be degradation within 9 weeks. Split tablets and intact tablets are stable after storage at room temperature for 9 weeks. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- Anticonvulsant dose: 10-20 mg/kg q8h PO. The higher dose may be needed in some dogs to control seizures.
- Neuropathic pain: Start with 5-15 mg/kg q12h PO and increase dose gradually to as high as 40 mg/kg q8-12h PO, if necessary.

**Cats**

- Anticonvulsant dose: 5-10 mg/kg q12h PO. The dose has been increased to 20 mg/kg q8-12h in some cats to control seizures.
- Neuropathic pain: 5-10 mg/kg q12h PO.

**Large Animal Dosage****Horses**

- Neuropathic pain: 2.5 mg/kg q12h PO.
- Laminitis: 2.5 mg/kg q8h, q12h, or q24h, and increase to higher doses as needed.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

Racing Commissioners International (RCI) Classification: 3

## Gamithromycin

gam-ith-roe-mye'sin

**Trade and Other Names:** Zactran

**Functional Classification:** Antibacterial

### Pharmacology and Mechanism of Action

Antibacterial related to the macrolide class of drugs. It is a 15-membered ring (like azithromycin and tulathromycin). Like other macrolides, it inhibits bacterial protein synthesis by binding to the ribosomal 50S subunit. It is considered bacteriostatic, but it may have bactericidal properties in vitro. Because of a positively charged molecule, it may penetrate gram-negative bacteria more easily than other macrolide antibiotics. The spectrum of activity for gamithromycin is limited to gram-positive bacteria and some gram-negative bacteria that cause respiratory diseases in cattle (e.g., *Mannheimia haemolytica*, *Mycoplasma*, and *Pasteurella multocida*). It also has activity against *Rhodococcus equi* and *Streptococcus equi* in horses. The half-life is long (e.g., 51-hour plasma half-life and 90-hour [4-day] half-life in lungs), which prolongs the drug concentration at the site of infection. The half-life is shorter in foals with a half-life of 39 hours and 64 hours in plasma and respiratory fluids, respectively. Other anti-inflammatory effects attributed to macrolide antibiotics may explain the clinical effects for respiratory infections, such as reduced inflammatory effects and cytokine expression in leukocytes.

### Indications and Clinical Uses

In cattle, gamithromycin is used for treatment of bovine respiratory disease (BRD) caused by *M. haemolytica*, *P. multocida*, and *Histophilus somni* (formerly *Haemophilus somnus*). It is also effective for treating infections caused by *Mycoplasma*. It also may be used for control of respiratory disease in beef and nonlactating dairy cattle at high risk of developing BRD (metaphylaxis) associated with *M. haemolytica* and *P. multocida*. In horses, clinical studies are not available, but experimental studies indicate that it may have efficacy for treating infections caused by *Streptococcus equi* and *Rhodococcus equi*.

### Precautionary Information

#### Adverse Reactions and Side Effects

Serious adverse reactions have not been observed. Injection-site reactions are possible in some animals, with swelling or irritation at the injection site.

#### Contraindications and Precautions

No specific contraindications have been reported.

#### Drug Interactions

No drug interactions have been reported.

### Instructions for Use

In cattle, administer as a single subcutaneous injection in the neck. In horses, an injection IM can be administered every 6-7 days to maintain effective concentrations in respiratory fluids.

### Patient Monitoring and Laboratory Tests

Clinical and Laboratory Standards Institute (CLSI) break point for susceptibility is  $\leq 4.0$  mcg/mL.

### Formulations

- Gamithromycin is available in a 150-mg/mL solution for injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage**

- No small animal doses have been established.

**Large Animal Dosage****Cattle**

- 6 mg/kg SQ (neck) as a single injection (2 mL per 110 pounds).

**Pigs**

- Not recommended.

**Horses**

- 6 mg/kg IM, administered every 7 days if needed.

**Regulatory Information**

No milk withdrawal times are established; do not use in lactating dairy cattle and do not use in female dairy cattle 20 months of age or older.

Do not treat cattle within 35 days of slaughter. No withdrawal period has been established for young prurminating calves; do not use in veal calves.

**Gemfibrozil**

jem-fih'broe-zil

**Trade and other names:** Lopid

**Functional classification:** Antihyperlipidemic agent

**Pharmacology and Mechanism of Action**

Gemfibrozil is an agent that lowers cholesterol, reduces plasma triglyceride and very-low-density-lipoprotein (VLDL), and increases high-density lipoproteins (HDL). Mechanism results from inhibition of peripheral lipolysis and reduced hepatic extraction of free fatty acids.

**Indications and Clinical Uses**

It is used for treatment of hyperlipidemia. It has been used in dogs for treatment of some hyperlipidemia syndromes, but the efficacy has not been reported.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects have not been reported in animals.

**Contraindications and Precautions**

No reported contraindications in animals.

**Drug Interactions**

No drug interactions are reported for animals.

**Instructions for Use**

Used primarily in people to treat hyperlipidemia, but it is used occasionally in dogs. Clinical studies have not been performed in animals.

**Patient Monitoring and Laboratory Tests**

Monitor cholesterol concentrations.

## Formulations

- Gemfibrozil is available in 600-mg tablets in the U.S., and 300-mg capsules (Canada only).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 7.5 mg/kg q12h PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

# Gentamicin Sulfate

jen-tah-mye'sin sul'fate

**Trade and other names:** Gentocin, Garasol, Garacin, and generic

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Aminoglycoside antibiotic. Action is to inhibit bacteria protein synthesis via binding to 30S ribosome. Gentamicin is bactericidal in a concentration-dependent manner. It has a broad spectrum of activity that includes most bacterial isolates in animals, including staphylococci and gram-negative bacilli of the *Enterobacteriaceae*. It is not very active against streptococci and anaerobic bacteria. The pharmacokinetics have been studied in many domestic and exotic animal species. The half-life is typically 1-2 hours in mammals, and the volume of distribution is approximately 0.2-0.3 L/kg. Clearance is via glomerular filtration.

## Indications and Clinical Uses

Gentamicin has a rapid, bactericidal action and is indicated for acute serious infections, such as those caused by gram-negative bacilli. Gentamicin has been administered IM, SQ, and IV. It is not absorbed after oral administration, and this use is restricted to labeled use in pigs. Gentamicin, like other aminoglycosides, can be used with beta-lactam antibiotics because it broadens the spectrum when used with drugs such as penicillins, ampicillin, or cephalosporins. Although gentamicin is generally active against most gram-negative bacilli, amikacin is more consistently active against resistant strains. The only approved use in food animals is oral treatment in pigs for swine dysentery.

## Precautionary Information

### Adverse Reactions and Side Effects

Nephrotoxicity is the most dose-limiting toxicity. Ensure that patients have adequate fluid and electrolyte balance during therapy. Electrolyte depletion will increase the risk of nephrotoxicity. High levels of calcium and protein in the diet will decrease the risk of nephrotoxicity. Ototoxicity and vestibulotoxicity also are

possible, but have not been reported in animals. With high doses, neuromuscular toxicity is possible, although rare.

### **Contraindications and Precautions**

Do not administer to animals with compromised renal function, renal insufficiency, kidney disease, or renal failure. There should be adequate renal clearance for clearance of gentamicin. Use in young animals is accepted, except higher doses may be necessary.

### **Drug Interactions**

When used with anesthetic agents, neuromuscular blockade is possible. Do not mix in vial or syringe with other antibiotics. Ototoxicity and nephrotoxicity are potentiated by loop diuretics such as furosemide.

## **Instructions for Use**

Dosing regimens are based on sensitivity of organisms. Some studies have suggested that once-daily therapy (combining multiple doses into a single daily dose) is as efficacious, and possibly more effective compared to administration more than once per day. The once daily treatment is also safer because of less kidney exposure, as multiple treatments. Activity against some bacteria (e.g., *Pseudomonas aeruginosa*) is enhanced when combined with a beta-lactam antibiotic, such as ceftazidime. Nephrotoxicity is increased with persistently high trough concentrations.

## **Patient Monitoring and Laboratory Tests**

Susceptibility testing: The CLSI minimum inhibitory concentration (MIC) break point for susceptibility is  $\leq 2$  mcg/mL. Monitor blood urea nitrogen (BUN), creatinine, and urine for evidence of renal toxicity. Blood levels can be monitored to measure for problems with systemic clearance. When monitoring trough levels in patients that are administered gentamicin once per day, the trough levels should be near or below the limit of detection. Alternatively, measure half-life from samples taken at 1 hour and 2-4 hours postdosing. Clearance should be approximately equal to the glomerular filtration rate (GFR) ( $>1.0$  mL/kg/min), and half-life should be less than 2 hours.

## **Formulations**

- Gentamicin is available in a 50- and 100-mg/mL solution for injection, a 50-mg/mL oral solution for pigs and a 5 mg/mL injection for turkeys.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Gentamicin is soluble in water. Do not mix with other drugs, especially in a vial, syringe, or fluid administration set. Inactivation may occur. Avoid long-term storage in plastic containers.

## **Small Animal Dosage**

### **Dogs**

- 2-4 mg/kg q8h or 9-14 mg/kg q24h SQ, IM, or IV.
- Once-daily administration is usually the preferred interval.

### **Cats**

- 5-8 mg/kg q24h SQ, IM, or IV.
- Once-daily administration is usually the preferred interval.

## **Large Animal Dosage**

### **Horses**

- Adult: 4-6.6 mg/kg q24h IM or IV.
- Foals younger than 2 weeks: 12-14 mg/kg q24h IM or IV.

**Pigs**

- 15 mg/kg for young pigs and 10 mg/kg for older pigs, once daily, SQ or IM.
- Colibacillosis, swine dysentery: 1.1-2.2 mg/kg for 3 days in drinking water.

**Calves**

- Younger than 2 weeks: 12-15 mg/kg q24h IV or IM.
- Adult cattle: 5-6 mg/kg q24h IM or IV.

**Regulatory Information**

With the exception of licensed products for pigs, aminoglycosides should not be administered to food animals because of residue concerns.

Withdrawal time for pigs: 3 days for meat at 1.1 mg/kg PO and 40 for days meat at 5 mg/kg IM; 14 days for meat at 5 mg/kg PO.

If gentamicin is administered systemically to cattle, an extended withdrawal time is necessary because of persistence of residues in the kidney. FARAD recommends 18 months. After systemic administration of 5 mg/kg, milk withdrawal time should be 5 days. If gentamicin is administered intramammarily (500 mg per quarter), a milk withdrawal time of at least 10 days and a meat withdrawal time of 180 days should be used.

Contact FARAD for additional information at 1-888-USFARAD (1-888-873-2723).

**Glipizide**

glip-ih'zide

**Trade and other names:** Glucotrol

**Functional classification:** Antidiabetic agent, hypoglycemic agent

**Pharmacology and Mechanism of Action**

Sulfonylurea oral hypoglycemic agent. This drug acts to increase secretion of insulin from beta cells of the pancreas, probably by interacting with sulfonylurea receptors on beta cells or by inhibiting adenosine triphosphate (ATP)-sensitive potassium channels on the pancreatic beta cells, which increases insulin secretion. These drugs also may increase sensitivity of existing insulin receptors. Studies in cats showed that glipizide had a half-life of 17 hours and effective plasma concentration for 50% efficacy ( $EC_{50}$ ) of 70 mcg/mL.

**Indications and Clinical Uses**

Glipizide is used as oral treatment in the management of diabetes mellitus, particularly in cats. The response rate in cats is approximately 44%-65% (some reports are 30% or lower). The response rate in dogs is poor. It has been more common to administer the sulfonylurea class of drugs in animals than other oral hypoglycemic drugs because they have had better efficacy. Glipizide is the most common of this class used in animals. Other oral hypoglycemic drugs include acetohexamide, chlorpropamide, glyburide (DiaBeta, Micronase), gliclazide, and tolazamide. Metformin is of the biguanide class of oral drugs for diabetes and has not had efficacy as high as glipizide in cats.

Glipizide transdermal absorption from a pluronic transdermal gel (pluronic organogel [PLO]) vehicle is poor in cats (<20%) and inconsistent. This route is not recommended.

**Precautionary Information****Adverse Reactions and Side Effects**

It may cause dose-related vomiting, anorexia, increased bilirubin, and elevated liver enzymes in some cats (15%). It may exacerbate deposits of amyloid in the feline pancreas and increase the loss of pancreatic beta cells. Glipizide may cause hypoglycemia, but less so than insulin. In people, increased cardiac mortality is possible, but this has not been reported in cats.

**Contraindications and Precautions**

Many cats do not respond and will require insulin therapy. Do not rely on glipizide in cats that are not stable or if they are dehydrated or debilitated.

**Drug Interactions**

Many drug interactions have been reported in people. It is not known if these occur in animals. Use cautiously with beta blockers, antifungal drugs, anticoagulants, fluoroquinolones, sulfonamides, and others.

**Instructions for Use**

Oral hypoglycemic agents are successful in people only for noninsulin-dependent diabetes. There has been only limited use in animals. Because response to oral hypoglycemic agents in cats is unpredictable, it is recommended to use a trial first of at least 4 weeks. If the cat responds, the drug can be continued; otherwise, insulin may be indicated. Feed cats a high-fiber diet when using oral hypoglycemic agents. Transdermal glipizide (5-mg dose) in a PLO gel was evaluated in cats. Although the transdermal formulation produced a modest change in glucose concentrations, systemic absorption was only 20%.

**Patient Monitoring and Laboratory Tests**

Monitor blood glucose levels to determine if the drug is effective. Monitor liver enzymes. It may increase alanine transaminase (ALT) and alkaline phosphatase.

**Formulations**

- Glipizide is available in 5- and 10-mg tablets.

**Stability and Storage**

Store glipizide in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- No effective dose available.

**Cats**

- 2.5-7.5 mg/cat q12h PO. Usual dose is 2.5 mg/cat initially, then increase to 5 mg/cat q12h.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Glucosamine Chondroitin Sulfate

gloo-koe'seh-meen + kahn-droy'ten sul'fate

**Trade and other names:** Cosequin, Glyco-Flex, and generic brands

**Functional classification:** Nutritional supplement

### Pharmacology and Mechanism of Action

Glucosamine is an amino sugar synthesized from glucose and glutamine. It is a source of glucosamine-6-phosphate and n-acetylglucosamine. It is an intermediate compound, converted to an ester that is incorporated into articular cartilage. Therefore it is a direct precursor in the formation of glycosaminoglycans in cartilage. Glucosamine is usually administered as a combination of glucosamine HCl and chondroitin sulfate. Other forms include glucosamine sodium sulfate and glucosamine potassium sulfate. Glucosamine has been promoted to stimulate synthesis of synovial fluid, inhibit degradation, and improve healing of articular cartilage. Additional information is available in the section on chondroitin sulfate. Bioavailability studies have produced varying results depending on formulation, assay technique, and species. Oral absorption of glucosamine has varied, ranging from 12% in dogs to only 2.5% (125 mg/kg) or 6% (20 mg/kg) in horses. Although in vitro studies have demonstrated benefits to articular cartilage, some studies have questioned whether oral glucosamine is absorbed systemically intact to a high enough extent to provide these benefits. Oral absorption may be affected by the form administered because glucosamine sulfate may be better absorbed than glucosamine hydrochloride.

### Indications and Clinical Uses

Glucosamine is used primarily for treatment of degenerative joint disease and is usually found in formulations in combination with chondroitin sulfate. (See "Chondroitin sulfate" for additional details.) Analyses of published clinical studies in dogs have concluded that there is a moderate level of evidence to indicate some benefit in osteoarthritis, but results may be inconsistent among studies. Benefits of treatment in horses with lameness also have been reported from oral administration of chondroitin-glucosamine supplements. There is a lack of supporting evidence that systemic administration is effective for reducing recurrent urinary tract infections in animals (via a beneficial effect on bladder mucosa). These compounds are regulated as dietary supplements that modify disease and are not regulated as drugs.

### Precautionary Information

#### Adverse Reactions and Side Effects

In some animals, soft stools and intestinal gas have been reported. In experimental rodents, injections of glucosamine can cause hyperglycemia, insulin resistance, and a decrease in the metabolic action of insulin via the hexosamine pathway. However, the clinical relevance of these findings has not been shown. Clinical studies in dogs have shown that short-term (21 days) administration of glucosamine does not affect glycemic control or cause diabetes mellitus in dogs. Otherwise, adverse effects have not been reported, although hypersensitivity is possible.

#### Contraindications and Precautions

The safety of glucosamine has not been established in diabetic animals or obese animals that may be prone to developing diabetes. Otherwise, there are no known precautions.



**Drug Interactions**

No drug interactions are reported. Glucosamine- and chondroitin-containing products may be used safely with NSAIDs.

**Instructions for Use**

Doses are based primarily on empiricism and manufacturer's recommendations. There are few published trials of efficacy or dose titrations available to determine optimal dose. Doses listed are general recommendations and may vary among products. Glucosamine hydrochloride is more bioavailable than glucosamine sulfate. Products may vary in their stability, purity, and potency. Use products from a reputable supplier.

**Patient Monitoring and Laboratory Tests**

No routine patient monitoring is necessary. There is no evidence that glucosamine administration will increase serum glucose. Glucosamine is produced by glucose in the body, but this is an irreversible reaction.

**Formulations**

- Several formulations are available. Veterinarians are encouraged to carefully examine product label to ensure proper strength. One product (Cosequin) is available as regular-strength ("RS") and double-strength ("DS") capsules. Regular strength contains 250 mg glucosamine, 200 mg chondroitin sulfate, mixed glycosaminoglycans, 5 mg manganese, and 33 mg manganese ascorbate. The DS tablets contain double of each of these amounts. Products for horses contain 3.3 g per scoop, equal to 1800 mg glucosamine and 570 mg chondroitin.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Products may vary in stability and potency.

**Small Animal Dosage**

- General dosing requirements for glucosamine: 22 mg/kg/day PO, and increased to 44 mg/kg/day PO in patients that do not initially respond. Alternatively, a better response may be anticipated by starting with the higher dose.
- Many preparations are administered in combination with chondroitin. For general dosing, use the Cosequin RS and DS strength as a general guide.

**Dogs**

- 1-2 capsules per day, and 2-4 capsules for large dogs.

**Cats**

- 1 capsule daily.

**Large Animal Dosage****Horses**

- 12 mg/kg glucosamine + 3.8 mg/kg chondroitin sulfate twice daily PO for 4 weeks, then 4 mg/kg glucosamine + 1.3 mg/kg chondroitin sulfate thereafter. It is common to initiate treatment in horses with a higher dose of 22 mg/kg glucosamine + 8.8 mg/kg chondroitin sulfate daily PO.

**Regulatory Information**

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

## Glyburide

glye'byoor-ide

**Trade and other names:** DiaBeta, Micronase, Glynase, and Glibenclamide (British name)

**Functional classification:** Antidiabetic agent, hypoglycemic agent

### Pharmacology and Mechanism of Action

Glyburide is a sulfonylurea oral hypoglycemic agent; it is also known as glibenclamide. This drug acts to increase secretion of insulin from the pancreas, probably by interacting with sulfonylurea receptors on beta cells or by interfering with ATP-sensitive potassium channels on pancreatic beta cells, which increases secretion of insulin. These drugs also may increase sensitivity of existing insulin receptors. It is used as oral treatment in the management of diabetes mellitus, particularly in cats. The response rate is approximately 40%. Sulfonylurea drugs include glipizide (Glucotrol) and glyburide (DiaBeta, Micronase). Metformin is of the biguanide class of oral drugs for diabetes.

**G**

### Indications and Clinical Uses

Oral hypoglycemic agents are successful in people only for noninsulin-dependent diabetes. There has been only limited use in animals. Glyburide is not effective in dogs, but has been used in some cats. Some cats may initially respond to oral hypoglycemic agents but eventually need insulin treatment. Similar drugs include acetohexamide, chlorpropamide, glipizide, gliclazide, and tolazamide. There is more experience with glipizide than with other drugs, and it should be used as the first choice (see “Glipizide” section for more details).

### Precautionary Information

#### Adverse Reactions and Side Effects

It may cause dose-related vomiting, anorexia, increased bilirubin, and elevated liver enzymes in some cats. Glyburide causes hypoglycemia, but less so than insulin. In people, increased cardiac mortality is possible.

#### Contraindications and Precautions

There are no known contraindications in animals.

#### Drug Interactions

No drug interactions are reported for animals. Many drug interactions have been reported in people. It is not known if these occur in animals because clinical use has been rare. Use cautiously with beta blockers, antifungal drugs, anticoagulants, fluoroquinolones, and sulfonamides.

### Instructions for Use

Because response to oral hypoglycemic agents in cats is unpredictable, it is recommended to use a trial first of at least 4 weeks. If the cat responds, the drug can be continued. Otherwise, insulin may be indicated. Feed cats a high-fiber diet when using oral hypoglycemic agents.

### Patient Monitoring and Laboratory Tests

Monitor blood glucose levels to determine if the drug is effective. Monitor liver enzymes.

**Formulations**

- Glyburide is available in 1.25-, 2.5-, and 5-mg tablets (DiaBeta and Micronase). Glynase is available in 1.5-, 3-, and 6-mg micronized tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- No effective doses have been reported.

**Cats**

- 0.2 mg/kg daily PO. Alternatively, start with 0.625 mg (one-half of 1.25 mg tablet) per cat once daily.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

No regulatory information is available. No withdrawal information is available.

**Glycerin**

glih'ser-in

**Trade and other names:** Generic

**Functional classification:** Diuretic, laxative

**Pharmacology and Mechanism of Action**

Glycerin has been administered to lower ocular pressure to treat acute glaucoma. However, IV mannitol is used more frequently for this purpose. Glycerin has been used as a laxative; it lubricates the stools and adds water to intestinal contents.

**Indications and Clinical Uses**

Glycerin is an osmotic agent that draws water into the intestine or renal tubule. Administered systemically, it acts as an osmotic diuretic agent, preventing water reabsorption from the renal tubules. Administered orally, it is not absorbed, but acts as an osmotic laxative, drawing water into the intestine.

**Precautionary Information****Adverse Reactions and Side Effects**

Glycerin may cause dehydration with frequent use or high doses.

**Contraindications and Precautions**

Do not administer to dehydrated animals.

**Drug Interactions**

No drug interactions are reported for animals.

**Instructions for Use**

Although glycerin may lower ocular pressure, other drugs are used to treat acute glaucoma.

## Patient Monitoring and Laboratory Tests

Monitor ocular pressures. Monitor electrolytes in treated animals.

## Formulations Available

- Glycerin is available in an oral solution or 40-mg/mL emulsion.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage (Dogs and Cats)

- 1-2 mL/kg q8h PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

## Glycopyrrolate

glye-koe-peer'oe-late

**Trade and other names:** Robinul-V

**Functional classification:** Anticholinergic

## Pharmacology and Mechanism of Action

Anticholinergic agent (blocks acetylcholine effect at muscarinic receptor), parasympatholytic. Glycopyrrolate produces atropinelike effects systemically. However, glycopyrrolate may have less effect on the central nervous system (CNS) compared to atropine because of lower penetration to CNS. It may produce a longer duration of action than atropine.

## Indications and Clinical Uses

Glycopyrrolate is used to inhibit vagal effects and increase heart rate in animals. It also will decrease respiratory, salivary, and gastrointestinal (GI) secretions. It may be used as an adjunct to anesthesia when it is necessary to override vagal stimulus. In horses, glycopyrrolate has a half-life of 7-19 hours, but varies depending on breed of horse.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are attributed to antimuscarinic (anticholinergic) effects. Side effects of therapy include xerostomia, ileus, constipation, tachycardia, and urine retention.

### Contraindications and Precautions

Do not use in patients with glaucoma, intestinal ileus, gastroparesis, or tachycardia.

### Drug Interactions

No specific drug interactions are reported for animals. However, it is expected that glycopyrrolate, like other anticholinergic drugs, will antagonize drugs that stimulate respiratory and GI secretions and GI motility.

**Instructions for Use**

Glycopyrrolate is often used in combination with other agents, particularly anesthetic drugs. Although some anesthetic agents such as alpha-2 agonists and opioids are associated with bradycardia, it is rarely necessary to administer anticholinergic agents such as glycopyrrolate to reduce the bradycardia.

**Patient Monitoring and Laboratory Tests**

Monitor heart rate during treatment.

**Formulations**

- Glycopyrrolate is available as a 0.2-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs and Cats**

- 0.005-0.01 mg/kg IV, IM, or SQ.

**Large Animal Dosage****Cattle and Horses**

- Use during anesthesia: 0.005-0.01 mg/kg IM or SQ or 0.0025- 0.005 mg/kg IV. A common dose is 1 mg per horse.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

**Gold Sodium Thiomalate**

gold soe'dee-um thye-oh-mah'late

**Trade and other names:** Myochrysine

**Functional classification:** Immunosuppressive

**Pharmacology and Mechanism of Action**

Used for gold therapy (chrysotherapy). Mechanism of action is unknown, but it may relate to immunosuppressive effect on lymphocytes or suppression of sulfhydryl systems.

**Indications and Clinical Uses**

Gold therapy is used primarily for immune-mediated diseases (such as dermatologic disease) in animals. In people, it has been used for rheumatoid arthritis. In animals, there is a lack of controlled clinical trials to document efficacy. Other immunosuppressive drugs are used more commonly.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects include dermatitis, nephrotoxicity, and blood dyscrasias.

**Contraindications and Precautions**

Use cautiously in animals with bone marrow suppression or renal disease.

**Drug Interactions**

Use with penicillamine will increase risk of hematologic adverse effects.

**Instructions for Use**

Clinical studies have not been performed in animals. Aurothioglucose generally is used more often than gold sodium thiomalate.

**Patient Monitoring and Laboratory Tests**

Complete blood count (CBC) should be monitored periodically during treatment.

**Formulations Available**

- **Note:** most forms of this drug are no longer approved and may not be available commercially. Gold sodium thiomalate is available in 10-, 25-, and 50-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs and Cats**

- 1-5 mg per animal IM first week, then 2-10 mg IM second week, and then 1 mg/kg once per week IM for maintenance.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Gonadorelin Hydrochloride, Gonadorelin Diacetate Tetrahydrate

goe-nad-oh-rell'in hye-droe-klor'ide, goe-nad-oh-rell'in dye-ass'eh-tate tet-ra-hye'drate

**Trade and other names:** Factrel, Fertagyl, Cystorelin, Fertilin, OvaCyst, GnRh, and LHRH

**Functional classification:** Hormone

**Pharmacology and Mechanism of Action**

Gonadorelin stimulates synthesis and release of luteinizing hormone (LH) and, to a lesser degree, follicle-stimulating hormone (FSH).

**Indications and Clinical Uses**

Gonadorelin is used to induce luteinization and ovulation in animals. Gonadotropin has been used to manage various reproductive disorders in which stimulation of ovulation is desired. In dairy cattle, it is used to treat ovarian follicular cysts.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects have not been reported in animals.

**Contraindications and Precautions**

Do not administer to pregnant animals. Extreme care should be used by people, particularly women, handling this medication. Human exposure may pose a risk to pregnant women.

**Drug Interactions**

No drug interactions in animals are reported.

**Instructions for Use**

For treatment of dairy cattle, with the diacetate tetrahydrate form, administer 100 mcg per cow as a single IM or IV injection for treatment of ovarian cysts. For the hydrochloride formulation, administer 100 mcg IM for the treatment of cystic ovaries (ovarian follicular cysts) in cattle to reduce the time to first estrus. In dairy cows, it may be used with dinoprost tromethamine or cloprostenol injection to synchronize estrous cycles to allow fixed-time artificial insemination (FTAI) in lactating dairy cows.

**Patient Monitoring and Laboratory Tests**

Monitor treated cattle for ovulation.

**Formulations**

- Gonadorelin is available in 50-mcg gonadorelin diacetate tetrahydrate per mL (equivalent to 43 mcg/mL of gonadorelin) or 50-mcg gonadorelin (as hydrochloride) in aqueous solution.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- 50-100 mcg/dog/day q24-48h IM.

**Cats**

- 25 mcg/cat once IM.

**Large Animal Dosage****Cattle**

- 100 mcg/cow IM or IV once. (Equivalent to approximately 2 mL per cow for gonadorelin diacetate tetrahydrate.) In lactating dairy cows 100–200 mcg/cow (2–4 mL) may be used, IM.

**Regulatory Information**

No withdrawal times are necessary (zero days).

**Gonadotropin, Chorionic**

go-nad-o-tro'pin, kor-ee-ahn'ik

**Trade and other names:** Profasi, Pregnyl, A.P.L., Follutein, Ferti-Cept, Chortropin, Chorulon, Improvest.

**Functional classification:** Hormone

## Pharmacology and Mechanism of Action

Gonadotropin is also referred to as *human chorionic gonadotropin* (hCG). The action of hCG is identical to that of LH.

## Indications and Clinical Uses

Gonadotropin is used to induce luteinization in animals. It has been used to manage various reproductive disorders where stimulation of ovulation is desired. In cows it is used for treatment of nymphomania (frequent or constant heat) due to cystic ovaries.

In pigs it is used for induction of fertile estrus (heat) in prepuberal (non-cycling) gilts or for induction of estrus in healthy weaned sows experiencing delayed return to estrus. It is also used in pigs for the temporary immunological castration (suppression of testicular function) and reduction of boar taint in intact male pigs intended for slaughter.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals.

#### Contraindications and Precautions

Do not administer to pregnant animals. Extreme care should be used by people, particularly women, handling this medication. Human exposure may pose a risk to pregnant women.

#### Drug Interactions

No specific drug interactions are reported.

## Instructions for Use

When used in horses, most ovulate 32-40 hours after treatment. In cows, it may be repeated in 14 days if the animal's behavior or rectal examination of the ovaries indicates the necessity for re-treatment. In pigs use only in gilts over 5½ months old and weighing at least 85 kilograms (185 pounds). Delayed return to estrus is most prevalent after the first litter. The effectiveness has not been established after later litters. Delayed return to estrus often occurs after periods of adverse environmental conditions, and sows mated after such conditions may farrow smaller than normal litters.

## Patient Monitoring and Laboratory Tests

Monitor treated patients for signs of luteinization and estrus.

## Formulations

- hCG and the cattle formulation is available in 5000-, 10,000-, and 20,000-unit vials for injection to be diluted in 10 mL of diluent. Swine formulation consists of 400 units serum gonadotropin and 200 chorionic gonadotropin as a freeze-dried powder to be reconstituted with 5 milliliters of sterile aqueous diluent.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 22 units/kg q24-48h IM or 44 units once IM.

### Cats

- 250 units/cat once IM.

## Large Animal Dosage

### Horses

- Ovulation induction: 2500-5000 units per mare IM or IV.



**Cattle (cows):**

- 10,000 units as a single, deep intramuscular injection. 500 to 2,500 units for intrafollicular injection. 2,500 to 5,000 units intravenously.

**Pigs (sows):**

- Conditions of use: 400 units serum gonadotropin with 200 units chorionic gonadotropin per 5 milliliters dose per animal, subcutaneously.

**Regulatory Information**

No regulatory information is available for food animals. A tolerance for residues of gonadotropin in uncooked edible tissues of cattle or of fish is not required. Because of low risk of residues, no withdrawal times are suggested.

## Granisetron Hydrochloride

grah-nih'seh-tron hye-droe-klor'ide

**Trade and other names:** Kytiril

**Functional classification:** Antiemetic

### Pharmacology and Mechanism of Action

Antiemetic drug from the class of drugs called *serotonin antagonists*. These drugs act by inhibiting serotonin (5-HT, type 3) receptors. During chemotherapy, 5-HT may be released from injury to the GI tract that stimulates vomiting centrally, which is blocked by this class of drugs. These drugs also have been used to treat vomiting from other forms of gastroenteritis. Other serotonin antagonists used for antiemetic therapy include granisetron, ondansetron, dolasetron, azasetron, and tropisetron.

### Indications and Clinical Uses

Granisetron, like other serotonin antagonists, is used primarily as an antiemetic during chemotherapy, for which it generally has been superior to other drugs in efficacy. It may be administered prior to chemotherapy to prevent nausea and vomiting. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

**Adverse Reactions and Side Effects**

None reported in dogs or cats. These drugs have little affinity for other serotonin receptors.

**Contraindications and Precautions**

No contraindications reported in animals.

**Drug Interactions**

No interactions are reported. It may be used with cancer chemotherapy agents.

### Instructions for Use

There have been only limited uses of this class of antiemetic drugs in veterinary patients. Most doses have been extrapolated from human uses.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Griseofulvin is available in 1-mg tablets and 1-mg/mL injection, and 0.5 mg/mL oral solution.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Discard opened vial after 30 days. Compounded solutions are stable in various fluids for 24 hours. Oral compounded formulations have been prepared in juices, syrups, and flavorings and were stable for 14 days.

## Small Animal Dosage

### Dogs and Cats

- 0.01 mg/kg IV or 0.02 mg/kg PO. (Oral doses have been extrapolated from people: 2 mg/person PO as single dose).

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No regulatory information is available for food animals. Because of low risk of residues, no withdrawal times are suggested.

## Griseofulvin

grizs-ee-oh-ful'vin

**Trade and other names:** Microsize: Fulvicin U/F, Grisactin, and Grifulvin; ultramicrosize: Fulvicin P/G and Gris-PEG

**Functional classification:** Antifungal

## Pharmacology and Mechanism of Action

Antifungal drug. After systemic administration, griseofulvin is deposited in the keratin precursor cells of the skin and hair. It is rapidly taken up into these tissues within 4-8 hours or 48-72 hours (depending on the study) after administration. Once it is incorporated into these cells, mitosis of the fungal cells is inhibited by effects on the mitotic spindle, and eventually fungal cells are killed.

## Indications and Clinical Uses

Griseofulvin is one of the drugs of choice when systemic treatment is needed for dermatophyte infections caused by *Microsporum* spp. and *Trichophyton* spp. in dogs and cats. It is sometimes used in combination with topical therapy. Griseofulvin is not effective for the treatment of yeasts or bacteria. At least 4 weeks, and sometimes 3 months or more, are needed for successful therapy. Its use has been replaced by azole antifungal drugs in many cases (itraconazole, fluconazole, etc.). It also has a predilection to accumulate in inflammatory sites of the skin and may be effective for treating some noninfectious, inflammatory dermatoses other than dermatomycosis. Because of the frequent use of azole antifungals (e.g., fluconazole, itraconazole) the use of griseofulvin has declined.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects in animals include teratogenicity in cats, anemia and leukopenia in cats, anorexia, depression, vomiting, and diarrhea. In cats, feline immunodeficiency virus (FIV) infection may increase the risk of bone marrow toxicosis. Whether the

bone marrow problems are caused by high doses or this is an idiosyncratic (non-dose related) reaction is not understood. These effects resolve in cats when treatment is stopped, but irreversible idiosyncratic pancytopenia has been reported.

### Contraindications and Precautions

Do not administer to pregnant cats. Caution should be used when administering griseofulvin to cats with viral infections (FIV) because this may exacerbate bone marrow effects.

### Drug Interactions

Griseofulvin is an enhancer of cytochrome P450 drug enzymes. Therefore other concurrent drugs may be metabolized and cleared more quickly if given with griseofulvin.

## Instructions for Use

A wide range of doses has been reported. Doses listed here represent the current consensus. Oral absorption is favored in the presence of fat, and administration of the drug with a high-fat meal can tremendously enhance the extent of absorption. Two formulations are available: microsize and ultramicrosize. Administration of a formulation made up of fine particles also will increase absorption. Veterinary formulations are generally composed of microsize preparations, and this is reflected in the dosage regimens. If the ultramicrosized preparations are used, the dose may be decreased by half. Shake oral suspension well before using. Consider 25 mg/kg q12h initially, and then increase to 50-60 mg/kg q12h for problem cases.

## Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow toxicity.

## Formulations

- Griseofulvin is available in 125-, 250-, and 500-mg microsize tablets; 25-mg/mL oral suspension; 125-mg/mL oral syrup; and 125-, and 250-mg, ultramicrosized tablets. It is also available as microsize griseofulvin powder in 15-gram pouches that contain 2.5 grams of the active ingredient.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Griseofulvin is insoluble in water, but is soluble in alcohol.

## Small Animal Dosage

### Dogs

- Microsize: 25 mg/kg q12h PO, up to a maximum dose of 50-60 mg/kg q12h. Start with 25 mg/kg q12h PO and then increase to 50-60 mg/kg q12h PO for refractory cases.
- Ultramicrosize: 30 mg/kg/day in divided treatments PO.

### Cats

- Microsize formulation: 25 mg/kg q12h, PO.

## Large Animal Dosage

### Horses

- Dermatophytosis: 5.6 mg/kg q24h of the oral microsize powder, which may be mixed with feed. Treatment should be continued for minimum of 10 days.

## Regulatory Information

No regulatory information is available for food animals. Because of potential for teratogenic effects, do not administer to food animals.

## Growth Hormone

**Trade and other names:** Somatrem, Somatropin, Protropin, Humatrope, and Nutropin

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Growth hormone, also known as *hCG*. It is administered to correct growth hormone deficiency in animals. Somatrem is a biosynthetic somatropin.

### Indications and Clinical Uses

Growth hormone is used to treat growth hormone deficiencies. The use is rare in veterinary medicine.

### Precautionary Information

#### Adverse Reactions and Side Effects

Growth hormone is diabetogenic in all animals. Excess growth hormone causes acromegaly.

#### Contraindications and Precautions

No contraindications reported in animals.

#### Drug Interactions

No drug interactions are reported in animals.

### Instructions for Use

There is only limited clinical experience in animals. Dose form must be reconstituted with sterile diluent before use.

### Patient Monitoring and Laboratory Tests

Monitor glucose periodically during treatment.

### Formulations

- Growth hormone is available in 5- and 10-mg/vial (1 mg is equal to 3 units).

### Stability and Storage

Prepared solution is stable if refrigerated for 14 days. Otherwise, it is stable for only 24 hours.

### Small Animal Dosage

#### Dogs and Cats

- 0.1 units/kg three times a week for 4-6 weeks SQ or IM. (Usual human pediatric dose is 0.18-0.3 mg/kg/week SQ or IM.)

### Large Animal Dosage

- No large animal doses have been reported.

### Regulatory Information

Do not administer to animals that produce food.

## Guaifenesin

gwyeh-fen'eh-sin

**Trade and other names:** Glyceryl guaiacolate, Guaiphenesin, Gecolate, Guailaxin, Glycotuss, Hytuss, Glytuss, Fenesin, Humibid LA, and Mucinex

**Functional classification:** Expectorant; muscle relaxant

### Pharmacology and Mechanism of Action

Guaifenesin, which is also known as glyceryl guaiacolate, is a compound that has been an older traditional therapy for treating cough in people, although the efficacy has been questioned for this effect. For respiratory disease, it is administered orally to produce an expectorant effect. This effect is presumably via stimulation of vagal transmission to produce more viscous bronchial secretions.

As an anesthetic adjunct, it is used as a preanesthetic with barbiturates and other injectable anesthetic agents. It is a central-acting skeletal muscle relaxant and causes sedation and relaxation via depression of nerve transmission. A distinct advantage is that it provides profound muscle relaxation without adverse cardiovascular and respiratory depression associated with other anesthetic agents. Pharmacokinetic information is limited, but half-life in ponies is 60-84 minutes and 60-108 minutes in horses. Duration of action in horses is approximately 30 minutes.

### Indications and Clinical Uses

Guaifenesin is administered IV (particularly in large animals) as an adjunct to anesthesia. Most often, it is used prior to induction of general anesthesia in horses. An example of this use in horses is "GKX," which is 1000-2000 mg ketamine, 500 mg xylazine, and 5% guaifenesin mixed and added to 1 liter to infuse at 2 mL/kg/hr IV or anesthesia. When administered with propofol to horses, it helped to prevent adverse anesthetic events that occur when propofol is administered as a sole agent.

Guaifenesin is also administered orally in animals as an expectorant. Supporting data for an expectorant effect are lacking. It may increase the volume and reduce the viscosity of secretions in the trachea and bronchi. It may also facilitate removal of secretions.

### Precautionary Information

#### Adverse Reactions and Side Effects

Minor leakage outside the vein from an IV injection does not cause tissue injury. However, thrombophlebitis from IV injection may occur. Hypotension may occur from high doses. Some hemolysis has been observed from IV infusion, but this is not significant at a concentration less than 15%. A vagal effect (e.g., stimulation of secretions) may occur when the drug is used as an expectorant.

#### Contraindications and Precautions

Do not administer IV if visible precipitate is observed.

Oral formulations for people (cough and cold remedies) may contain other ingredients such as dextromethorphan or decongestants (e.g., phenylephrine or pseudoephedrine). Do not use these combinations in animals sensitive to these drugs, and if possible, use only formulations that contain guaifenesin.

#### Drug Interactions

No significant drug interactions are reported. It has been safely used with acepromazine, xylazine, detomidine, ketamine, thiopental, and pentobarbital.

## Instructions for Use

For anesthetic purposes, 5% guaifenesin is prepared from powder (50 g/L) dissolved in sterile water. It dissolves more readily if the water is warm. Infusion of 110 mg/kg can produce transient recumbency, but usually it is administered with other agents. It can be administered with a variety of other anesthetic agents for the benefit of producing a more smooth induction in horses. One such combination is Equine “Triple-Drip” listed in the dosing section.

## Patient Monitoring and Laboratory Tests

Monitoring of animals during anesthesia (heart rate, rhythm, and respiratory rate) is suggested. Hypotension is possible; therefore blood pressure should be monitored.

## Formulations

- Guaifenesin is available in IV solutions that are prepared prior to infusion from powder to a 5% solution. It is also available in a 100- and 200-mg tablet; 600-mg extended-release tablets; and 20-mg/mL and 40-mg/mL oral solution. Human over-the-counter formulations may contain other ingredients such as dextromethorphan and decongestants.

## Stability and Storage

Guaifenesin is soluble in water and in alcohol. It is more soluble in warm water. It will precipitate if the temperature is 22° C or colder. It should be administered orally shortly after preparation because stability is short. However, 10% solutions have been stable for as long as 7 days. For IV use, it has been mixed with xylazine and ketamine without apparent loss of stability.

## Small Animal Dosage

### Dogs

- Expectorant: 3-5 mg/kg q8h PO.
- Anesthetic adjunct: 2.2 mL/kg/hr of a 5% solution intravenously. Administered with  $\alpha_2$  agonists and ketamine.

### Cats

- Expectorant: 3-5 mg/kg q8h PO.

## Large Animal Dosage

### Horses

- 2.2 mL/kg of a 5% solution (110 mg/kg) infused intravenously to horses prior to other anesthetic agents, such as ketamine. Guaifenesin solution may be infused rapidly.
- Constant-rate infusion (CRI): 2.2 mL/kg/hour of 5% solution (50 mg/mL).
- Induction dose (with propofol): 90 mg/kg IV administered over 3 minutes, followed by propofol 3 mg/kg IV bolus.
- Equine “triple-drip”: 1 liter of 5% guaifenesin in dextrose, mixed with 500 mg xylazine and 2 grams ketamine. Administer as 1.1 mL/kg for induction, and then 2-4 mL/kg/hr infusion, IV. Use yohimbine if necessary to speed recovery.

## Regulatory Information

Withdrawal time (extralabel): 3 days for meat and 48 hours for milk.

RCI Classification: 4

## Halothane

hal'oe-thane

**Trade and other names:** Fluothane

**Functional classification:** Inhalant anesthetic

### Pharmacology and Mechanism of Action

Inhalant anesthetic. Halothane is a multi-halogenated ethane. It is characterized by rapid induction and recovery, high potency, and few adverse effects. Like other inhalant anesthetics, the mechanism of action is uncertain. They produce generalized, reversible depression of the central nervous system (CNS). The inhalant anesthetics vary in their solubility in blood, their potency, and the rate of induction and recovery. Those with low blood/gas partition coefficients are associated with the most rapid rates of induction and recovery. Halothane has a vapor pressure of 243 mm Hg (at 20° C), a blood/gas partition coefficient of 2.3, and a fat/blood coefficient of 51. Because of high solubility in fat, its clearance from the body is slower than other agents.

### Indications and Clinical Uses

Halothane, like other inhalant anesthetics, is used for general anesthesia in animals. It has a minimum alveolar concentration (MAC) value of 1.04%, 0.87%, and 0.88% in cats, dogs, and horses, respectively. However, it is rarely used today and has been replaced by newer inhalant anesthetics (e.g., isoflurane) in many veterinary practices.

### Precautionary Information

#### Adverse Reactions and Side Effects

Like other inhalant anesthetics, halothane produces vasodilation and increased blood flow to cerebral blood vessels. This may increase intracranial pressure. Also like other inhalant anesthetics, it produces a dose-dependent myocardial depression, with accompanying decrease in cardiac output. It also depresses respiratory rate and alveolar ventilation. In addition, like other inhalant anesthetics, it increases the risk of ventricular arrhythmias, especially in response to catecholamines. Hepatotoxicity has been reported in people.

#### Contraindications and Precautions

Administer with caution to patients with cardiovascular problems.

#### Drug Interactions

No specific drug interactions. Use of other anesthetics in conjunction with halothane will lower the requirement for the halothane dose.

### Instructions for Use

Use of inhalant anesthetics requires careful monitoring. Dose is determined by depth of anesthesia.

### Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and rhythm and respiration during anesthesia.

### Formulations

- Halothane is available in a 250-mL bottle.

### Stability and Storage

Halothane is highly volatile and should be stored in a tightly sealed container.

**Small Animal Dosage**

- Induction: 3%
- Maintenance: 0.5%-1.5%

**Large Animal Dosage**

- MAC value: 1%

**Regulatory Information**

No withdrawal times are established for food animals. Clearance is rapid, and short withdrawal times are suggested. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

**Hemoglobin Glutamer (Oxyglobin)**

hee'moe-gloe-bin gloot'am-er

**Trade and other names:** Oxyglobin

**Functional classification:** Iron supplement, hemoglobin substitute

**Pharmacology and Mechanism of Action**

Hemoglobin glutamer (bovine) is used as oxygen-carrying fluid in dogs with varying causes of anemia. Oxyglobin is an ultrapurified polymerized bovine hemoglobin. The molecular weight is 64,000-500,000 (average 200,000). Osmolality is 300 mOsm/mL. Colloid osmotic pressure is higher than other colloids, with a colloid osmotic pressure of 43.3. Half-life in dogs is approximately 24 hours (range 18-43 hours). It is metabolized by macrophages, and 95% of a dose is eliminated in 5-9 days.

**Indications and Clinical Uses**

Hemoglobin glutamer has been used to treat anemia caused by blood loss, hemolysis, or decreased blood cell production. Although approved for dogs, it also has been used in cats. However, because of decreased availability from the manufacturer, the use has become infrequent.

**Precautionary Information****Adverse Reactions and Side Effects**

Circulatory overload is possible, especially with high doses and rapid administration. Patients at the most risk of circulatory overload are those with cardiac disease, respiratory disease, risk of hypertension, cerebral edema, oliguria/anuria caused by renal failure, and cats. Pulmonary hypertension has been observed because of depletion of nitric oxide (NO) and volume overload. Because cats are more sensitive to the adverse effects than dogs, lower dose rates should be used in cats. Other adverse effects have been skin and mucous membrane discoloration, vomiting, diarrhea, and anorexia. Discoloration of skin and mucous membranes can persist for 3-5 days.

**Contraindications and Precautions**

Hemoglobin glutamer should not be used in dogs with advanced heart disease. Administer with caution to cats because of an increased risk of pulmonary hypertension.

**Drug Interactions**

Do not administer with other drugs via the same infusion set. Do not mix with other drugs.



**Instructions for Use**

Administer using aseptic technique. In 5-7 days, 90% of dose is eliminated.

**Patient Monitoring and Laboratory Tests**

Use of Oxyglobin does not require cross-matching, but because these patients are usually critically ill, they should be monitored carefully. Monitoring packed cell volume (PCV) or hematocrit is not useful for assessing response to Oxyglobin therapy. Oxyglobin will interfere with other monitoring tests, such as blood chemistry analysis (colorimetric assays). Doses of 30 mL/kg are listed by the manufacturer, but many veterinarians use 10-15 mL/kg.

**Formulations**

- Hemoglobin glutamer is available in 13 g/dL polymerized hemoglobin of bovine origin in 60-mL and 125-mL single-dose bags. Availability from manufacturer may be limited.

**Stability and Storage**

At room temperature, hemoglobin glutamer has a 3-year shelf-life. Once opened, a 125-mL bag should be used within 24 hours because of oxidation of hemoglobin to methemoglobin. Do not freeze.

**Small Animal Dosage****Dogs**

- One-time dose of 10-30 mL/kg IV or up to a rate of 5-10 mL/kg/hr.

**Cats**

- One-time dose of 3-5 mL/kg IV, slowly. Maximum rate is 5 mL/kg/hr and not to exceed 13-20 mL/kg in 24 hours.

**Large Animal Dosage**

No doses reported. Do not use in race horses.

**Regulatory Information**

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested. However, hemoglobin glutamer (Oxyglobin) is prohibited to be on the premises of racing horses.

Racing Commissioners International (RCI) Classification: 2

**Heparin Sodium**

hep'ah-rin soe'dee-um

**Trade and other names:** Liquaemin and Hepalean (Canada)

**Functional classification:** Anticoagulant

**Pharmacology and Mechanism of Action**

Anticoagulant. Heparin produces its action by increasing antithrombin III-mediated inhibition of synthesis and activity of factor Xa. Heparin differs from low-molecular-weight heparin (LMWH) by an equal anti-factor Xa/anti-factor IIa ratio. Heparin has a ratio of 1:1, but the LMWHs have ratios of 2:1 or higher. In people, there is an advantage of LMWH over conventional heparin because the LMWHs have longer half-lives and less frequent administration is needed. However, this may not be an advantage for dogs and cats. Consult the description of LMWH for more information such as the sections on enoxaparin (Lovenox) and dalteparin (Fragmin).

## Indications and Clinical Uses

Heparin is administered to prevent and treat hypercoagulability disorders and prevent coagulation disorders such as thromboembolism, venous thrombosis, disseminated intravascular coagulopathy (DIC), and pulmonary thromboembolism. Use in specific situations in animals is primarily anecdotal or derived from the clinical experience in people. No outcome-based studies to evaluate efficacy have been published to support specific guidelines for therapy. Use for prevention of thrombosis in canine patients with immune-mediated hemolytic anemia has not been effective (50-300 units/kg SQ q6h), but when doses were adjusted based on anti-Xa activity, it was more effective, and doses in individual dogs was as high as 560 mg/kg q6h. In horses, it is used to prevent thrombosis in patients at risk, but efficacy has not been measured at the recommended doses.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects caused by excessive inhibition of coagulation result in bleeding. Heparin-induced thrombocytopenia, a problem in people, has not been cited as a problem in animals. If excessive anticoagulation and bleeding occur as a result of an overdose, protamine sulfate should be administered to reverse heparin therapy. Protamine should be administered by slow IV infusion. It complexes with heparin to form a stable, inactive compound.

### Contraindications and Precautions

Do not use in animals unless able to monitor bleeding because it may be life threatening. Do not inject intramuscularly because it may create a hematoma.

### Drug Interactions

Use cautiously in animals that are already receiving other drugs that can interfere with coagulation, such as aspirin and warfarin. Although a specific interaction has not been identified, use cautiously in animals that may be receiving certain chondroprotective compounds, such as glycosaminoglycans for treatment of arthritis.

## Instructions for Use

Dose adjustments should be performed by monitoring clotting times. For example, dose is adjusted to maintain activated partial thromboplastin time (APTT) at 1.5 to 2 times normal. For information on other forms of heparin, such as LMWHs, see sections on dalteparin or enoxaparin. Duration of anticoagulant effect may vary among patients, but in general, a 200-unit/kg dose in dogs has a duration of effect of approximately 6 hours.

In high-risk patients, doses used include 500 units/kg SQ or IM, followed by reduced doses such as those listed in dosing section q8-12h.

It also has been used to prepare heparinized saline solutions for flushing catheters. The advantage of using heparinized saline instead of regular saline for flushing saline has not been shown in clinical studies. However, the dose for providing this solution is listed in the dosing section.

## Patient Monitoring and Laboratory Tests

Monitor effect using APTT or anti-Xa activity. Dose is adjusted to maintain APTT at 1.5 to 2 times normal. Target range for anti-Xa activity is 0.35-0.70 units/mL. If anti-Xa activity is greater than 70 units/mL, reduce dose by 25%.

## Formulations

- Heparin sodium is available in 1000- and 10,000-units/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats (Low-Dose Prophylaxis)**

- 70 units/kg q8-12h SQ.
- To prepare heparinized saline solutions for IV use: the recommended mixture ranges from 0.25 to 10 units per mL of fluids. This is equivalent to adding 0.25 mL of heparin (1,000 units/mL concentration) per 1000 mL of fluids, or 1 mL heparin (10,000 units/mL concentration) per 1000 mL of fluids, respectively. (*Note: The advantage of adding heparin to fluid solutions for flushing IV catheters has not been demonstrated in clinical studies.*)

**Dogs**

- 100-200 units/kg IV loading dose, then 100-300 units/kg q6-8h SQ. Adjust dose via monitoring, and increase to 500-600 units/kg if necessary. In more severe cases, start with 500 units/kg SQ as initial dose, then administer 500 units/kg q12h.
- Constant-rate infusion (CRI): Loading dose of 100 units/kg IV, followed by CRI 18 units/kg/hour.

**Cats**

- 300 units/kg SQ q8h, and increase up to 500 units/kg if necessary.

**Large Animal Dosage**

- 125 units/kg SQ or IM q8-12h. (Lower doses of 80 units/kg SQ q12h also have been used in horses.)

**Regulatory Information**

No regulatory information is available for food animals. Because of low risk of residues, no withdrawal times are suggested.

**Hydralazine Hydrochloride**

hye-drahl'ah-zeen hye-droe-klor'ide

**Trade and other names:** Apresoline

**Functional classification:** Vasodilator

**Pharmacology and Mechanism of Action**

Vasodilator. Antihypertensive. Hydralazine relaxes vascular smooth muscle and reduces blood pressure. In arteriolar vascular beds, it relaxes vascular smooth muscle to reduce vascular resistance and improves cardiac output. The mechanism of action is not certain. It may generate NO or act via other smooth muscle-relaxing properties. The peak effect occurs approximately 3-5 hours after administration, and the duration of effect on blood vessels is approximately 12 hours.

**Indications and Clinical Uses**

Hydralazine is used to dilate arterioles and decrease cardiac afterload. It is primarily used for treatment of congestive heart failure (CHF), valvular disease of the heart, and other cardiovascular disorders characterized by high peripheral vascular resistance. It may be used with other cardiac drugs. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials

to document clinical effectiveness. However, its use is not as common as other vasodilator drugs, such as the angiotensin-converting enzyme (ACE) inhibitors.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are attributed to excess vasodilation and subsequent hypotension, which results in tachycardia. Hydralazine may dangerously decrease cardiac output. Allergic reactions (lupus-like syndrome) have been reported in people and are related to acetylator status but have not been reported in animals. Repeated use will activate the renin-angiotensin-aldosterone system (RAAS).

#### Contraindications and Precautions

Do not use in hypotensive animals.

#### Drug Interactions

No specific drug interactions are reported for animals. However, use cautiously with other drugs that may lower blood pressure.

### Instructions for Use

Use of hydralazine in heart failure may accompany other drugs, such as digoxin, pimobendan, and diuretics. Dosage in animals may be adjusted by monitoring blood pressure.

### Patient Monitoring and Laboratory Tests

Monitor patients for hypotension. Monitor blood pressure to adjust dose.

### Formulations

- Hydralazine is available in 10-, 25-, 50-, and 100-mg tablets and 20-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Exposure to light may change color and cause decomposition. Hydralazine is unstable. Mixing with juices, syrups, and flavorings may cause decomposition in as little as 24 hours.

### Small Animal Dosage

#### Dogs

- 0.5 mg/kg (initial dose); titrate to 0.5-2 mg/kg q12h PO.

#### Cats

- 2.5 mg/cat q12-24h PO.

### Large Animal Dosage

#### Horses

- 1 mg/kg q12h PO or 0.5 mg/kg IV as needed to reduce blood pressure.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Hydrochlorothiazide

hye-droe-klor-oh-thye'ah-zide

**Trade and other names:** HydroDIURIL, Hydrozide (for cattle), and generic

**Functional classification:** Diuretic

## **Pharmacology and Mechanism of Action**

Thiazide diuretic. Like other thiazide diuretics, it inhibits sodium reabsorption in distal renal tubules and causes urinary diuresis. Because thiazide diuretics act in the distal tubules (at the point where the most water has already been reabsorbed), their diuretic effects are not as great compared with loop diuretics such as furosemide.

## **Indications and Clinical Uses**

Like other thiazide diuretics, hydrochlorothiazide is used to increase excretion of sodium, potassium, and water. It also has been used as an antihypertensive. Because thiazide diuretics decrease renal excretion of calcium, they also have been used to treat uroliths containing calcium (calcium oxylate uroliths). Use in small animals has been primarily derived from anecdotal experience. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. In cattle, hydrochlorothiazide is approved for use in dairy cattle as an aid in the treatment of postparturient udder edema.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Hydrochlorothiazide may cause electrolyte imbalance such as hypokalemia.

#### **Contraindications and Precautions**

Do not use in patients with high serum calcium. Thiazide diuretics will prevent calcium excretion. When administered to dairy cattle, milk taken from dairy animals during treatment and for 72 hours (6 milkings) after the latest treatment must not be used for food.

#### **Drug Interactions**

Use carefully with other diuretics. It may enhance the effects of other diuretics and antihypertensive agents.

## **Instructions for Use**

Hydrochlorothiazide is not as potent as loop diuretics (e.g., furosemide). Clinical efficacy has not been established in veterinary patients.

## **Patient Monitoring and Laboratory Tests**

Monitor hydration status, electrolytes, and renal function. When used in cattle, animals should be regularly and carefully observed for early signs of fluid and electrolyte imbalance.

## **Formulations**

- Hydrochlorothiazide is available in 10- and 100-mg/mL oral solution and 25-, 50-, and 100-mg tablets. The combination of hydrochlorothiazide and spironolactone is Aldactazide. The cattle formulation is 25 mg/mL for injection.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## **Small Animal Dosage**

### **Dogs and Cats**

- 2-4 mg/kg q12h PO.

### **Cats**

- To decrease excretion of calcium in urine: 1 mg/kg q12h PO.
- Congestive heart failure: 1-2 mg/kg q12-24h PO.

## Large Animal Dosage

### Cattle

5 to 10 mL (125 to 250 milligrams) IV or IM, once or twice a day. After onset of diuresis treatment may be continued with an orally administered maintenance dose. For oral treatment use chlorothiazide boluses.

### Regulatory Information

Withdrawal time for cattle: 72 hour (6 milkings) milk withdrawal; no withdrawal time for slaughter is established. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Hydrocodone Bitartrate

hye-droe-koe'done bye-tar'trate

**Trade and other names:** Hycodan, Vicodin, Lortab, and generic

**Functional classification:** Antitussive, analgesic

### Pharmacology and Mechanism of Action

Opioid agonist, analgesic. Like other opioids, hydrocodone is an agonist for mu-opiate and kappa-opiate receptors on nerves and inhibits release of neurotransmitters involved with transmission of pain stimuli (such as substance P). Hydrocodone is metabolized to other metabolites, including hydromorphone, which has approximately 6x the potency of morphine. Central sedative and euphoric effects are related to mu-receptor effects in the brain. Other opiates used in animals include hydromorphone, codeine, oxymorphone, meperidine, and fentanyl. Hycodan contains homatropine, which is added to decrease abuse by people. Hydrocodone formulations used for antitussive action may also contain guaifenesin or acetaminophen. Hydrocodone is metabolized to hydromorphone in animals (e.g., dogs), and the pharmacologic effects may be attributed to hydromorphone. In dogs, after a dose of 0.5 mg/kg oral, plasma concentrations of hydromorphone in the analgesic range were maintained for 8 hours. In people the combinations of hydrocodone and acetaminophen (e.g., Vicodin) and hydrocodone and aspirin are often prescribed as oral treatments for pain.

### Indications and Clinical Uses

Hydrocodone is an opiate agonist that has antitussive, analgesic, and sedative properties. Studies in animals, especially dogs, have shown that hydrocodone is absorbed orally, and partially metabolized to hydromorphone and other metabolites that have analgesic properties. The analgesic properties of oral hydrocodone have not been tested in animals. Hydrocodone has been most often used in animals as an antitussive for symptomatic treatment of airway diseases, and many clinicians believe (anecdotally) that it is an effective antitussive. There are no antitussive preparations marketed for use in the US that do not contain atropine. (Canadian preparations may contain only hydrocodone.) It may also contain other ingredients for treating cough.

### Precautionary Information

#### Adverse Reactions and Side Effects

Like all opiates, side effects are predictable and unavoidable. Side effects include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses. Paradoxical excitement may occur in some animals.

**Contraindications and Precautions**

Do not use in patients that may be sensitive to opiate effects or experience dysphoria. Because preparations for oral use contain atropine, do not use in animals in which atropine may be contraindicated. Many formulations for treating pain in people contain hydrocodone and acetaminophen, or hydrocodone and aspirin. Acetaminophen-containing products should never be administered to cats.

**Drug Interactions**

No specific drug interactions are reported for animals.

**Instructions for Use**

Hydrocodone is combined with atropine in the product Hycodan. Atropine can decrease respiratory secretions, but probably does not exert significant clinical effects at doses in this preparation (1.5 mg homatropine per 5-mg tablet). There are many analgesic preparations for people that contain hydrocodone.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- There are many oral formulations for humans to treat pain that contain hydrocodone and other analgesics such as acetaminophen (e.g., Vicodin). Typically these preparations contain 5 mg hydrocodone and 500 mg acetaminophen. Hydrocodone is also available as an antitussive (Hydodan) in 5-mg tablets and 1-mg/mL syrup combined with homatropine in a concentration of 1.5 mg in tablets and 0.3 mg/mL in syrup, respectively. Formulations in Canada do not contain homatropine. The formulation of Zohydro-ER is an extended-release formulation (10-, 15-, 20-, 30-, 40-, and 50-mg tablets) approved for use in people for treating pain. Hysingla is an extended-release formulation for treating pain in people containing 20, 30, 40, 60, 80, 100, or 120 mg. These extended-release formulations provide extended duration for once- or twice-daily administration, but have not been evaluated for animals.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs**

- Antitussive dose: 0.5 mg/kg q8 hr PO. Increase the dose if needed for tracheal collapse in dogs, but not above the dose of 1.5 mg/kg.
- Analgesic dose: 0.5 mg/kg q8-12 hr PO.

**Cats**

- No dose has been established. Oral doses may be effective in cats, but caution should be used because many formulations contain acetaminophen.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

Hydrocodone is a Schedule II drug controlled by the Drug Enforcement Administration (DEA).

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 1

## Hydrocortisone

hye-droe-kor'tih-sone

**Trade and other names:** Hydrocortisone, Cortef and generic brands, Hydrocortisone sodium succinate, Solu-Cortef

**Functional classification:** Corticosteroid

### Pharmacology and Mechanism of Action

Glucocorticoid anti-inflammatory drug. Hydrocortisone has weaker anti-inflammatory effects and greater mineralocorticoid effects compared with prednisolone or dexamethasone. Hydrocortisone has properties that most closely resemble natural cortisol in the body. It is about 1/5 the potency of prednisolone and 1/25 the potency of dexamethasone. Anti-inflammatory effects are complex but are primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators.

**H**

### Indications and Clinical Uses

Hydrocortisone is used for anti-inflammatory effects and for glucocorticoid replacement therapy. It is not used as commonly as other corticosteroids such as prednisolone or dexamethasone, except when hormone replacement to mimic effects of cortisol is needed. Hydrocortisone sodium succinate is a rapid-acting injectable product that can be used when a prompt response is needed.

### Precautionary Information

#### Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic–pituitary–adrenal (HPA) axis suppression. Adverse effects include gastrointestinal (GI) ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and urinary tract infections (UTIs). In horses, additional adverse effects include risk of laminitis.

#### Contraindications and Precautions

Use cautiously in patients prone to ulcers or infection or in animals in which wound healing is necessary. Use cautiously in diabetic animals, animals with renal failure, or pregnant animals.

#### Drug Interactions

Glucocorticoids are often synergistic with other anti-inflammatory and immunosuppressive drugs. Administration of corticosteroids with nonsteroidal anti-inflammatory drugs (NSAIDs) will increase the risk of GI injury.

### Instructions for Use

Dose requirements are related to severity of disease. Typically for replacement therapy (such as in animals with hypoadrenocorticism) doses start at 1 mg/kg/day.

### Patient Monitoring and Laboratory Tests

Monitor electrolytes (sodium and potassium) in animals being treated for hypoadrenocorticism. Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform adrenocorticotrophic hormone (ACTH) stimulation test to monitor adrenal function.



**Formulations**

- Hydrocortisone is available in 5-, 10-, and 20-mg tablets, and hydrocortisone sodium succinate is available in various size vials for injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Hydrocortisone is slightly soluble in water and is soluble in alcohol. Degradation occurs at high pH above 7-9. Compounded suspensions have been stable for 30 days. Most compounded topical ointments and lotions are stable for 30 days.

**Small Animal Dosage****Dogs and Cats*****Hydrocortisone***

- Replacement therapy: 1-2 mg/kg q12h PO.
- Anti-inflammatory: 2.5-5 mg/kg q12h PO.

***Hydrocortisone Sodium Succinate***

- Shock: (not a recommended use) 50-150 mg/kg IV, for 2 doses, 8 hours apart.
- Anti-inflammatory: 5 mg/kg q12h IV.

**Large Animal Dosage****Horses**

- Hydrocortisone sodium succinate: 5 mg/kg q12h IV.

**Foals**

- Replacement therapy for critical illness: 1-3 mg/kg/day IV.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

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**Hydromorphone**

hye-droe-mor'fone

**Trade and other names:** Dilaudid, Hydrostat, and generic brands

**Functional classification:** Analgesic, opiate

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**Pharmacology and Mechanism of Action**

Opioid agonist, analgesic. Like other opiates, it binds to mu-opiate and kappa-opiate receptors on nerves and inhibits release of neurotransmitters involved with transmission of pain stimuli (such as substance P). Opiates also may inhibit release of some inflammatory mediators. Central sedative and euphoric effects are related to mu-receptor effects in the brain. Hydromorphone has similar qualitative properties as morphine, but is six or seven times more potent than morphine. In dogs, the half-life after IV administration was 70-80 minutes. Other opiates used in animals include morphine, codeine, oxymorphone, meperidine, and fentanyl. When oral hydrocodone is administered to animals, it is partially metabolized to hydromorphone (hydrocodone discussed above).

**Indications and Clinical Uses**

Hydromorphone is used in animals for analgesia and sedation and as an adjunct for anesthesia. In dogs and cats, it is used as a single agent or in combination with other agents. Hydromorphone is an opiate agonist, with effects similar to morphine.

However, it is more potent than morphine (6-7  $\times$ ) and should be used at lower doses. Because hydromorphone is less expensive than other opiates (e.g., oxymorphone), it is sometimes used instead of other drugs without evidence of superior efficacy. Hydromorphone is approximately half as potent as oxymorphone and five to seven times as potent as morphine. These drugs are equal in efficacy but, doses should be adjusted accordingly. Studies in dogs indicate that hydromorphone at equivalent doses is equal to oxymorphone for producing sedation in dogs. In cats, duration of effect (0.1 mg/kg) has been 6-7.5 hours, despite a relatively short plasma half-life of 1-1.5 hours.

### Precautionary Information

#### Adverse Reactions and Side Effects

Like all opiates, side effects from hydromorphone are predictable and unavoidable. Side effects from administration include sedation, panting, constipation, urinary retention, and bradycardia. In cats, the most common adverse effects are dysphoria, hypersalivation, and vomiting. Hyperthermia also has been observed in cats, but the mechanism is not known. In dogs, hydromorphone produces less histamine release than morphine administration and therefore may produce fewer histamine-related side effects.

Respiratory depression occurs with high doses. As with other opiates, a slight decrease in heart rate is expected. In most cases, this decrease does not have to be treated with anticholinergic drugs (e.g., atropine), but should be monitored. Tolerance and dependence occur with chronic administration. In horses, undesirable and even dangerous behavior actions can follow rapid IV opioid administration. Horses should receive a preanesthetic of acepromazine or an  $\alpha_2$  agonist.

#### Contraindications and Precautions

Cats and horses are more sensitive to excitement than other species. Monitor the body temperature in cats because hyperthermia may occur. Hydromorphone may cause bradycardia and atrioventricular (AV) block in some patients.

#### Drug Interactions

No significant interactions. Hydromorphone may be used with other anesthetics. If butorphanol is used concurrently, it may diminish the effects of hydromorphone by antagonizing mu-opiate receptors.

### Instructions for Use

Hydromorphone may be used interchangeably with morphine or oxymorphone, provided that doses are adjusted for potency differences. Administration to cats has been more effective when injected intravenously, rather than intramuscularly or subcutaneously, and resulted in faster onset with fewer adverse effects. Oral tablets and solution are available for human use, but use has not been reported for animals. The oral tablets of hydrocodone, which is metabolized partially to hydromorphone, are used more often when oral treatment is needed.

### Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, if necessary, atropine or glycopyrrolate can be administered. If serious respiratory depression occurs, the opioid can be reversed with naloxone. Monitor body temperature in cats. Hyperthermia has been observed in patients after anesthesia.

### Formulations

- Hydromorphone is available in 1-mg/mL oral solution; 2-, 4-, and 8-mg tablets; and 1-, 2-, 4-, and 10-mg/mL injection.

## 384 Hydroxyethyl Starch

- Exalgo is an extended-release formulation for people in 8-, 12-, and 16-mg tablets that allows for once-daily treatment. This formulation has not been evaluated in animals.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Hydromorphone is soluble in water. Compounded solutions in fluids have been stable for 30 days. It is a Schedule II drug and should be stored in a locked compartment.

### Small Animal Dosage

#### Dogs

- 0.22 mg/kg IM or SQ. Repeat every 4-6 hours or as needed for pain treatment.
- 0.1-0.2 mg/kg IV, repeated every 2 hours or as necessary. A dose of 0.1 mg/kg may be used with acepromazine as a preoperative sedative.

#### Cats

- 0.1-0.2 mg/kg SQ or IM, or 0.05-0.1 mg/kg IV q2-6h (as needed).
- Epidural dose: 0.05 mg/kg, diluted in saline to 0.2 mL/kg (1 mL per cat).

### Large Animal Dosage

#### Horses

- Epidural: 0.04 mg/kg diluted in 0.9% saline to 20 mL.
- No systemic doses have been reported.

### Regulatory Information

Hydromorphone is a Schedule II drug controlled by the DEA. Withdrawal times have not been established for food animals, but the elimination rate is rapid and a brief withdrawal time is suggested. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 1

## Hydroxyethyl Starch

**Trade and other names:** HES, hetastarch, Hespan, tetrastarch, and VetStarch (veterinary product)

**Functional classification:** Fluid replacement

### Pharmacology and Mechanism of Action

Hydroxyethyl starch is a synthetic colloid volume expander that is used to maintain vascular volume in animals with circulatory shock. It is a modified branched-chain glucose polymer derived from amylopectin sources such as potatoes, sorghum, or maize. The hydroxyethyl starch preparations include tetrastarch, hetastarch, and pentastarch. Hetastarch (6%) has an average molecular weight of 200 kDa (kilodaltons) and a colloid osmotic pressure of approximately 30. Pentastarch (10%) has an average molecular weight of 200 kDa and a colloid osmotic pressure of 30-60. Tetrastarch (VetStarch) 6% has a molecular weight of 130 kDa and a colloid osmotic pressure of 36. The number of molecular substitutions determine whether it is hetastarch, pentastarch, or hexastarch. Hetastarch has the most molecular substitutions and tends to remain longest in the vasculature. Hetastarch is cleared much more slowly than tetrastarch. Although hetastarch is prevented from hydrolysis in blood, thereby prolonging intravascular expansion, this property also is associated with accumulation in the reticuloendothelial system, skin, liver, and kidney.

## Indications and Clinical Uses

Hydroxyethyl starch is used primarily to treat acute hypovolemia and shock. It is administered intravenously in acute situations in which rapid restoration of circulating volume is needed. Hydroxyethyl starch solutions have a duration of effective volume expansion of 12-48 hours.

### Precautionary Information

#### Adverse Reactions and Side Effects

Most of the serious adverse effects reported, such as kidney injury and coagulation abnormalities, have been observed in human studies and have not been documented with clinical use in veterinary medicine. The use in people has become controversial and caution is advised when using these products in animals, with attention to the most commonly reported problems in people. Hetastarch may cause allergic reactions and hyperosmotic kidney injury. Hydroxyethyl starch solutions may affect platelet function and produce coagulation abnormalities at clinically relevant doses for up to 24 hours. The high-molecular-weight hetastarch may alter coagulation and alter viscoelastic measurements and fibrinolysis. Do not use in patients with bleeding problems or preexisting coagulopathies. High-molecular-weight products (10% solutions) have molecular weight more than 200 kDa (kilodaltons) and are associated with higher risk of kidney injury. Tetrastarch solutions also may have less tendency to cause coagulopathies than hetastarch. Therefore the current recommendation is to use tetrastarch solutions of 6% and reduced molecular weight (130 kDa).

#### Contraindications and Precautions

Do not use in animals with bleeding problems (coagulopathies) or active hemorrhage. Do not use in animals with known kidney disease.

#### Drug Interactions

Hydroxyethyl starch is compatible with most fluid solutions.

## Instructions for Use

Suspend in saline (0.9%) or 5% dextrose solution for use. Administer slowly in 5-mL/kg increments to small animals, then reassess and increase the dose to rates listed in the dosing section. Hydroxyethyl starch solutions are used in critical care situations and infused via CRI.

## Patient Monitoring and Laboratory Tests

Monitor patient's hydration status and blood pressure during administration. Monitor heart rate and rhythm, and observe patients for evidence of bleeding. Monitor kidney parameters and discontinue use if signs of kidney injury are observed. Monitor for signs of coagulopathy or platelet dysfunction, and discontinue if there are bleeding problems. Administration of hydroxyethyl starch solutions may increase patient's amylase for 2-3 days.

## Formulations

- Hydroxyethyl starch is available in 6% injectable solution as an approved veterinary formulation (tetrastarch, VetStarch). Several other hydroxyethyl starch solutions (hetastarch, pentastarch, hexastarch) in concentrations of 6% and 10% are available.

## Stability and Storage

Hydroxyethyl starch is stable in the original packaging and is compatible with most fluid administration sets.

**Small Animal Dosage****Dogs**

- Small volume resuscitation: 5 mL/kg IV.
- Large volume resuscitation: 5-15 mL/kg, IV.
- CRI: 10-20 mL/kg/day IV (0.4-0.8 mL/kg/hr). Maximum dose is 33-50 mL/kg/day.

**Cats**

- Resuscitation: 2-5 mL/kg IV.
- CRI: 5-10 mL/kg/day IV (0.2-0.4 mL/kg/hr).

**Large Animal Dosage****Horses**

- 8-10 mL/kg bolus dose or CRI 0.5-1 mL/kg/hr.

**Regulatory Information**

No regulatory information is available for food animals. Because of low risk of residues, no withdrawal times are suggested.

**Hydroxyurea**

hye-droks'ih-yoo-ree-ah

**Trade and other names:** Droxia and Hydrea (Canada)

**Functional classification:** Anticancer agent

**Pharmacology and Mechanism of Action**

Antineoplastic agent. Hydroxyurea is a cell-cycle-dependent agent, acting primarily at the S-phase of mitosis. The exact mechanism of action is uncertain, but it may interfere with DNA synthesis in cancer cells. The specific effects on red blood cells (RBCs) occur because of the activity on hemoglobin.

**Indications and Clinical Uses**

In people, hydroxyurea is used for treatment of sickle cell anemia and occasionally various carcinomas. In animals, it has been used in combination with other anticancer modalities for treatment of certain tumors. In animals, one of the uses has been treatment of polycythemia vera.

**Precautionary Information****Adverse Reactions and Side Effects**

Because of only limited use in veterinary medicine, no adverse effects have been reported. In people, hydroxyurea causes leukopenia, anemia, and thrombocytopenia.

**Contraindications and Precautions**

Avoid use in pregnant animals.

**Drug Interactions**

No specific drug interactions are reported for animals.

**Instructions for Use**

Hydroxyurea has been used on a limited basis in veterinary medicine. Most of the use is empirical or extrapolated from human medicine.

## Patient Monitoring and Laboratory Tests

Monitor complete blood count (CBC) in treated animals.

## Formulations

- Hydroxyurea is available in 200-, 300-, 400-, and 500-mg capsules.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 50 mg/kg PO once daily, 3 days/week.

### Cats

- 25 mg/kg PO once daily, 3 days/week.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Hydroxyzine Hydrochloride

hye-droks'ih-zeen

**Trade and other names:** Atarax, Vistaril

**Functional classification:** Antihistamine

## Pharmacology and Mechanism of Action

Antihistamine ( $H_1$  blocker) of the piperazine class. Like other antihistamines, hydroxyzine acts by blocking the  $H_1$  receptor and suppresses inflammatory reactions caused by histamine. The  $H_1$  blockers have been used to control pruritus and skin inflammation, rhinorrhea, and airway inflammation. Hydroxyzine also has sedative properties and other calming effects on the CNS that are not related to the antihistamine effects.

Another antihistamine, cetirizine, is an active metabolite of hydroxyzine. In dogs, most of the antihistamine effect of the administration of hydroxyzine is from the formation of cetirizine, which occurs readily after IV and oral administration.

## Indications and Clinical Uses

In animals, it has been used to treat pruritus. Efficacy in animals for treating pruritus is low. Although it has been shown in experimental animals to suppress histamine response, it has not been consistently effective relieving pruritus in dogs with atopic dermatitis. Other uses include allergic airway disease and rhinitis. However, efficacy is not established for these uses. In people, additional uses include treatment of anxiety and psychoneurosis and as a sedative before and after general anesthesia.

## Precautionary Information

### Adverse Reactions and Side Effects

Sedation is the most common side effect. It is the result of inhibition of histamine N-methyltransferase. Sedation may also be attributed to the blocking of other CNS receptors such as those for serotonin, acetylcholine, and alpha-receptors.

Antimuscarinic effects (atropine-like effects), such as dry mouth and decreased GI secretions, also are common.

**Contraindications and Precautions**

No contraindications reported in animals.

**Drug Interactions**

No specific drug interactions are reported for animals.

**Instructions for Use**

Clinical studies have shown hydroxyzine to be somewhat effective for treatment of pruritus in dogs, but efficacy rates are low.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Hydroxyzine hydrochloride is available in 10-, 25-, and 50-mg tablets; 2-mg/mL oral syrup; and 25-mg/mL injection. It is also available in a pamoate form (Vistaril) in 25-, and 50-mg capsules.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Hydroxyzine is soluble in water. Compounded formulation with syrups was stable for 14 days.

**Small Animal Dosage****Dogs**

- 2 mg/kg q8-12h IM or PO.

**Cats**

- Effective doses have not been established (see section on cetirizine for dosing information for cats)

**Large Animal Dosage****Horses**

- Hydroxyzine pamoate 500 mg per horse, orally, twice daily (efficacy not established).

**Regulatory Information**

No regulatory information is available for food animals. Because of low risk of residues, no withdrawal times are suggested.

RCI Classification: 2

**Hyoscyamine**

hye-oh-sye'ah-meen

**Trade and other names:** Levsin

**Functional classification:** Anticholinergic

**Pharmacology and Mechanism of Action**

Anticholinergic agent (blocks acetylcholine effect at muscarinic receptor), parasympatholytic.

## Indications and Clinical Uses

Hyoscyamine is an anticholinergic drug with actions similar to atropine and related drugs. It will produce an antiemetic effect to decrease vomiting associated with motion sickness and some GI diseases. It is indicated in animals for conditions in which it is important to block parasympathetic responses. It has been used to decrease GI motility and secretions, decrease salivation, and increase heart rate (to treat bradycardia).

### Precautionary Information

#### Adverse Reactions and Side Effects

Side effects include xerostomia, ileus, constipation, tachycardia, and urine retention.

#### Contraindications and Precautions

Do not use in patients with glaucoma, intestinal ileus, gastroparesis, or tachycardia.

#### Drug Interactions

Do not mix with alkaline solutions. Hyoscyamine will antagonize the effects of any cholinergic drugs administered (e.g., metoclopramide).

## Instructions for Use

Hyoscyamine is used primarily in dogs for cardiovascular and GI diseases.

## Patient Monitoring and Laboratory Tests

Monitor heart rate and intestinal motility during treatment.

## Formulations

- Hyoscyamine is available in 0.125-mg tablets, 0.375-mg extended-release tablets, and 0.025-mg/mL solution.

## Stability and Storage

Store in a tightly sealed container at room temperature.

## Small Animal Dosage

### Dogs

- 0.003-0.006 mg/kg q8h PO.

### Cats

- No doses have been established for cats.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Do not use in animals that produce food.

Withdrawal time: None established in US (manufacturer of large animal products lists 0 days for milk and meat), but is listed as 14 days for meat and 3 days for milk in the UK.



## **Ibuprofen**

eye-byoo-proe'fen

**Trade and other names:** Motrin, Advil, Nuprin, and generic

**Functional classification:** Nonsteroidal anti-inflammatory drug (NSAID)

### **Pharmacology and Mechanism of Action**

Like other NSAIDs in this class, ibuprofen produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclo-oxygenase (COX) enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy gastrointestinal (GI) tract, renal function, platelet function, and other normal physiologic functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Ibuprofen is not selective for either COX-1 or COX-2. It is approved for human use, and experience with this drug in veterinary medicine is limited.

Pharmacokinetics have been studied in a variety of animals. In horses, the half-life is approximately 60-90 minutes. Oral absorption is high in horses (80%-90%), regardless of the dose form used, including a compounded paste. Ibuprofen was 90%-100% absorbed when administered orally to dairy goats.

### **Indications and Clinical Uses**

Ibuprofen is not approved for any animals in veterinary medicine. There are drugs in small animals that have been safer for the GI tract and are preferred. Use of ibuprofen in dogs is discouraged because of high risk of GI ulceration. It has been used for musculoskeletal inflammation in horses and ruminants. Administration of 25 mg/kg IV to cows reduced some systemic variables in endotoxin-induced mastitis.

In horses, doses of 10-25 mg/kg have been used, but clinical trials of efficacy have not been reported.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Vomiting, severe GI ulceration, and hemorrhage have been reported in dogs. Like other NSAIDs, renal injury caused by decrease in renal perfusion has occurred with ibuprofen. Ibuprofen may inhibit platelets in animals.

#### **Contraindications and Precautions**

Safe doses have not been established for dogs and cats. Do not administer to animals prone to GI ulcers. Do not administer with other ulcerogenic drugs such as corticosteroids.

#### **Drug Interactions**

No specific drug interactions are reported. However, like other NSAIDs, ulcerogenic effects are potentiated when administered with corticosteroids. Ibuprofen, like other NSAIDs, may interfere with the action of diuretics, such as furosemide and angiotensin-converting enzyme (ACE) inhibitors.

### **Instructions for Use**

Avoid use in dogs. Safe dosages for other species have not been established, although there has been some extra-label use in ruminants and horses.

## Patient Monitoring and Laboratory Tests

Monitor for signs of GI ulcers. Monitor renal function during therapy.

## Formulations

- Ibuprofen is available in 200-, 400-, 600-, and 800-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ibuprofen has been compounded in alcohol (ethanol) and propylene glycol solutions without loss of stability. It is poorly soluble in water. Ibuprofen has been compounded as an oral paste for horses without compromising the oral absorption.

## Small Animal Dosage

### Dogs and Cats

- Safe dose not established.

## Large Animal Dosage

### Horses

- 25 mg/kg q8h PO, up to 6 days.

### Ruminants

- 14-25 mg/kg/day PO.

## Regulatory Information

No withdrawal times are established for animals intended for food. For extralabel use with withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

Racing Commissioners International (RCI) classification: 4

# Imidocarb Hydrochloride and Imidocarb Dipropionate

im-id'oh-carb hye-droe-klor'ide

**Trade and other names:** Imizol

**Functional classification:** Antiprotozoal

## Pharmacology and Mechanism of Action

Imidocarb is an aromatic diamidine. It inhibits nucleic acid metabolism in susceptible organisms and produces anticholinergic effects. Antimicrobial activity against protozoal organisms accounts for its clinical use. It appears to particularly affect the erythrocyte stages of the parasite by inhibition of inositol entry into infected erythrocytes.

## Indications and Clinical Uses

Imidocarb has been used in animals to treat intracellular tick-borne pathogens. It has been used to treat *Babesia* infections and has been used to treat haemobartonellosis in cats caused by the organisms *Mycoplasma haemofelis* and *Mycoplasma haemominutum*. Imidocarb also has been used to treat *Cytauxzoon felis* infections in cats and ehrlichial infections in dogs and cats. In horses, it has been used to treat equine piroplasmiasis caused by *Theileria equi* and *Babesia caballi*.

## Precautionary Information

### Adverse Reactions and Side Effects

No toxic reactions were observed in trials with experimental cats. Transient pain or discomfort occurs in most animals at the site of injection. Posttreatment vomiting may occur in 10%-40% of animals. Transient increase in liver enzymes (alanine

aminotransferase [ALT], aspartate aminotransferase [AST]) may occur. After IM injection, it remains in tissues for a prolonged period. Adverse effects from high doses include kidney injury (tubular necrosis) and acute hepatic necrosis.

Two forms are available: dipropionate salt and hydrochloride salt. The hydrochloride salt is more irritating when injected intramuscularly.

In horses, anticholinesterase effects are common, resulting in increased endogenous acetylcholine, which causes sweating, agitation, bronchoconstriction, salivation, colic signs, intestinal spasmodic reactions, and diarrhea. These effects are transient and not life threatening, but treat these signs with atropine if they are severe. To prevent these signs, one may pretreat with atropine (0.02 mg/kg IV, glycopyrrolate (0.0025 mg/kg IV), or N-butyloscopolammonium bromide (scopolamine).

### Contraindications and Precautions

Administer intramuscularly only. Do not administer intravenously. Donkeys and mules are more susceptible to adverse effects than are horses, and treatment should be avoided in these animals.

### Drug Interactions

No drug interactions have been reported.

## Instructions for Use

Use of imidocarb has been limited in animals. Most protocols are established from small clinical trials or extrapolation from human use.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Imidocarb compounded formulations are available from some pharmacies. Imidocarb dipropionate is available as 12% solution (120 mg/mL).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Cats

- 5 mg/kg IM two doses administered 14 days apart.

### Dogs

- (*Ehrlichia canis*): 6.6 mg/kg IM, (0.25 mL per 10 pounds) two doses administered 14 days apart.

## Large Animal Dosage

### Horses

- 4.4 mg/kg once, or 2.2 mg/kg IM for 2 doses, with 24- to 48-hour interval between doses. Inject in different locations. To eradicate *B. caballi*, inject 4 mg/kg IM for 4 treatments every 72 hours. Consider pretreating with anticholinergic drug (see [adverse effects](#) section).

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Imipenem-Cilastatin

ih-mih-pen'em + sye-lah-stat'in

**Trade and other names:** Primaxin

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Imipenem + cilastatin is a beta-lactam antibiotic of the carbapenems class with a broad spectrum of activity. The mechanism of action is similar to the other beta-lactam antibiotics, which is to inactivate the penicillin-binding proteins (PBP) and cause cell wall lysis, or interfere with cell wall formation. The carbapenems are capable of binding to a specific PBP (PBP-1) that results in more rapid lysis compared to other beta-lactams. This results in greater bactericidal activity and a longer postantibiotic effect. Carbapenems have a broad spectrum of activity and are among the most active of all antibiotics. The spectrum includes gram-negative bacilli, including *Enterobacteriaceae* and *Pseudomonas aeruginosa*. It also is active against most gram-positive bacteria, except methicillin-resistant strains of *Staphylococcus* and *Enterococcus*. Compared to imipenem, meropenem and doripenem are slightly more active. Cilastatin has no antibacterial activity, but it is a specific inhibitor of renal dipeptidase (dehydropeptidase, DHP-I). Therefore cilastatin blocks renal tubular metabolism of imipenem and improves urinary recovery of imipenem.

Dosage regimens have been developed from pharmacokinetic studies in dogs, cats, and horses. In cats it was absorbed from IM and SQ injection 90%-100%. The half-life was 1.2, 1.4, and 1.5 hours from IV, IM, and SQ injection, respectively, and produced a peak concentration of 6.5 and 4 mcg/mL from IM and SQ, respectively. In dogs, the half-life was 0.8, 0.9, and 1.54 hours from IV, IM, and SQ injection, respectively. Absorption from IM and SQ injection was 145% and 159%, respectively, producing a peak concentration of 13.2 and 8.8 mcg/mL, respectively. Thus in both dogs and cats, the SQ administration prolongs the half-life, which is helpful for a time-dependent agent such as imipenem. In horses, the elimination half-life from IV administration was 70 minutes, with volume of distribution of 0.4-0.5 L/kg.

### Indications and Clinical Uses

Imipenem is used primarily for infections caused by bacteria resistant to other drugs. It is especially valuable for treating resistant infections caused by *P. aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*. Although active against gram-positive bacteria such as staphylococci (but not methicillin-resistant strains), other drugs should be used for gram-positive infections. Meropenem and doripenem are newer drugs in the class of carbapenems and have some advantages with respect to activity and convenience of administration. Meropenem is often preferred for administration to dogs and cats because it is easier to administer and more stable.

### Precautionary Information

#### Adverse Reactions and Side Effects

Allergic reactions may occur with beta-lactam antibiotics. With rapid infusion or in patients with renal insufficiency, neurotoxicity may occur. Neurotoxicity in animals has included tremors, nystagmus, and seizures. Nephrotoxicity is possible, but imipenem is combined with cilastatin to decrease renal metabolism. Vomiting and nausea are possible. Intramuscular injections can cause painful reactions.

**Contraindications and Precautions**

Use cautiously in patients prone to seizures. Seizures may be more likely in patients with renal failure.

**Drug Interactions**

No known drug interactions. Do not mix with other drugs in vial.

**Instructions for Use**

Efficacy studies have not been determined in animals. Recommendations are based on extrapolation of studies performed in humans. Reserve the use of this drug for resistant, refractory infections. Observe manufacturer's instructions carefully for proper administration. When the vial is initially reconstituted, it should not be given intravenously. It first must be diluted in a suitable IV fluid solution (at least 100 mL). For IV administration, add to IV fluids. After reconstitution in vial, 250 or 500 mg should be added to not less than 100 mL of fluids and given intravenously over 30-60 minutes. Intravenous fluid solutions are stable for 48 hours if refrigerated or 8 hours at room temperature. For IM administration, 2 mL lidocaine (1%) may be added to decrease pain from injection. The suspension is stable for only 1 hour. In some hospitals, the IV solution has been diluted in fluids and administered SQ without any sign of injection-site reactions (usually 8-14 mL per injection in dogs).

**Patient Monitoring and Laboratory Tests**

Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) break points for sensitive organisms are  $\leq 1$  mcg/mL. Most veterinary pathogens have minimum inhibitory concentration (MIC) values less than 1.0 mcg/mL.

**Formulations**

- Imipenem + cilastatin is available in 250- and 500-mg vials for injection. Intramuscular suspension is available in 500- and 750-mg vials.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. After reconstitution, it is stable for 4 hours at room temperature and 24 hours refrigerated. Do not freeze IV fluid solutions. Slight yellow discoloration is acceptable, but discard if color turns brown.

**Small Animal Dosage****Dogs**

- 5 mg/kg q6-8h IV, IM, or SQ.

**Cats**

- 5 mg/kg q6-8h IV or IM, or q8h for SQ.

**Large Animal Dosage****Horses**

- 10-20 mg/kg q6h by slow IV (10-minute) infusion.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Imipramine Hydrochloride

im-ip'rah-meen hye-droe-klor'ide

**Trade and other names:** Tofranil and generic brands

**Functional classification:** Behavior modification

### Pharmacology and Mechanism of Action

Tricyclic antidepressant (TCA) drug. Imipramine, like others in this class, is used in people to treat behavior problems, anxiety and depression. Action is via inhibition of uptake of serotonin and norepinephrine at presynaptic nerve terminals. Other TCA drugs used in animals include clomipramine and amitriptyline.

### Indications and Clinical Uses

Like other TCAs, imipramine is used in animals to treat a variety of behavioral disorders, including obsessive-compulsive disorders, separation anxiety, and inappropriate urination. There have been fewer studies of efficacy with imipramine than with clomipramine or amitriptyline. Generally, other behavior-modifying drugs such as selective serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine) or other TCAs (clomipramine) are preferred by behavior experts for treating small animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Multiple side effects are associated with TCAs, such as antimuscarinic effects (dry mouth and rapid heart rate) and antihistamine effects (sedation). Overdoses can produce life-threatening cardiotoxicity.

#### Contraindications and Precautions

Use cautiously in patients with heart disease.

#### Drug Interactions

Do not use with other behavior-modifying drugs, such as serotonin reuptake inhibitors. Do not use with monoamine oxidase inhibitors (MAOIs) such as selegiline.

### Instructions for Use

Doses are primarily based on empiricism. There are few controlled efficacy trials available for animals to compare with other drugs in this class. There may be a 2- to 4-week delay after initiation of therapy before beneficial effects are seen.

### Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm in treated animals. Like other TCAs, imipramine may decrease total  $T_4$  and free  $T_4$  concentrations in dogs.

### Formulations

- Imipramine is available in 10-, 25-, and 50-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Although imipramine has been compounded for veterinary use, the potency and stability have not been evaluated for compounded products.

**Small Animal Dosage****Dogs**

- 2-4 mg/kg q12-24h PO.

**Cats**

- 0.5-1 mg/kg q12-24h PO.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

Do not administer to animals intended for food.

RCI classification: 2

**Indomethacin**

in-doe-meth'ah-sin

**Trade and other names:** Indocin

**Functional classification:** Nonsteroidal anti-inflammatory drug

**Pharmacology and Mechanism of Action**

Nonsteroidal anti-inflammatory drug and analgesic. Like other NSAIDs, indomethacin produces potent analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the COX enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal physiologic functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Indomethacin is considered a prototype for a nonselective drug because it inhibits equally both COX-1 and COX-2. Indomethacin is approved for human use, and experience with this drug in veterinary medicine is limited. It acts to inhibit COX that synthesizes prostaglandins, but may have other anti-inflammatory effects (such as effects on leukocytes). In people, is used primarily for short-term treatment of moderate pain and inflammation.

**Indications and Clinical Uses**

Indomethacin, like other NSAIDs, has been used to treat pain and inflammation in people. However, it has not been used often in clinical veterinary medicine because other safer, approved drugs are available. Indomethacin is used as a prototypical nonselective COX-1 and COX-2 blocker in research. In dogs, the high risk of GI ulceration prohibits its routine use.

**Precautionary Information****Adverse Reactions and Side Effects**

Indomethacin has produced severe GI ulceration and hemorrhage in dogs. Like other NSAIDs, it may cause renal injury via inhibition of renal prostaglandins.

**Contraindications and Precautions**

Do not use in dogs or cats.

### Drug Interactions

Like other NSAIDs, several drug interactions are possible. Nonsteroidal anti-inflammatory drugs have the potential to interfere with the action of diuretics, such as furosemide, and ACE inhibitors, such as enalapril. Corticosteroids, when used with NSAIDs, will increase the risk of ulceration.

### Instructions for Use

Use cautiously, if at all, because safe doses have not been determined for clinical use in animals.

### Patient Monitoring and Laboratory Tests

Monitor for signs of GI toxicity (hemorrhage, ulcers, and perforation).

### Formulations

- Indomethacin is available in 20-, 25-, 40- and 50-mg capsules and 5-mg/mL oral suspension.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Indomethacin is practically insoluble in water, but is soluble in ethanol. It decomposes in alkaline conditions and is maximally stable at pH 3.75.

### Small Animal Dosage

#### Dogs and Cats

- Safe dose has not been established.

### Large Animal Dosage

- No large animal doses have been reported.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI classification: 4

## Insulin

in'syoo-lin

**Trade and other names:** ProZinc, Lente insulin, Ultralente insulin, Regular insulin, Glargine insulin, NPH insulin, Caninsulin, Protamine zinc insulin (PZI), Humulin (human insulin), Vetsulin is porcine insulin zinc suspension (veterinary), and PZI Vet (veterinary protamine zinc insulin)

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Insulin has multiple effects associated with utilization of glucose. It is critical to the management of diabetes mellitus in dogs and cats. Oral hypoglycemic agents are used in people; however, there is no good evidence to support their use in preference to insulin therapy in cats, and the oral hypoglycemic agents are ineffective in dogs. If owners cannot give injections, glipizide is the only oral hypoglycemic agent with evidence to support the use as a sole therapy for cats (see glipizide section for more information).



Dog insulin is identical to pork insulin, but dog insulin differs from beef insulin by 3 amino acids. Cat, insulin is similar to beef insulin with only one amino acid difference. Despite an amino acid difference in cats, there have not been problems with anti-insulin antibodies in treated cats. Most beef-pork insulin combinations for humans have been discontinued and are not usually available for veterinary use. Human-recombinant insulins can be used in dogs and cats with the same effects as natural insulin. Insulin is available in several preparations:

1. **Regular insulin:** Short acting. Peak is 1-5 hours, and duration is 4-10 hours. Usually used for short-term management such as for diabetic ketoacidosis.
2. **Neutral protamine hagedorn** (isophane, also called NPH): 100 units/mL. A human-recombinant insulin of crystalline suspension with protamine zinc that is intermediate acting. Peak is 2-10 hours in dogs and 2-8 hours in cats with a duration of action of 4-24 hours in dogs and 4-12 hours in cats (but usually 2-3 hours in cats). Not usually recommended for cats because of short duration.
3. **Lente insulin.** Peak is 2-10 hours in dogs and 2-8 hours in cats with a duration of action of 4-24 hours in dogs and 4-12 hours in cats. Addition of protamine or zinc to insulin will produce a crystallized insulin in suspension that has a longer absorption rate than dissolved insulin. The lente forms of insulin control their duration by the size of the crystal. For example, semilente is practically amorphous, whereas ultralente has large crystals, and lente is a combination of ultralente and semilente.
4. **Ultralente insulin:** Peak is 4-16 hours in dogs and 2-14 hours in cats and has a duration of 8-28 hours in dogs and 12-24 hours in cats. It is poorly absorbed in cats and usually not recommended. Human products have been discontinued.
5. **Vetsulin:** Also known as Caninsulin. Vetsulin is a U-40 porcine insulin, identical to canine insulin in amino acid content, and is a lente insulin of aqueous zinc suspension of crystalline and noncrystalline insulins. It produces a shorter peak of activity (4 hours) and duration than PZI insulin. This product has been temporarily suspended by some sources, but has returned to the market.
6. **Protamine-zinc insulin (PZI):** Developed from recombinant human insulin and longer acting. Veterinary form is called ProZinc in a 40-unit/mL form for cats. The forms used in animals are identical to the forms marketed for people. Response and pharmacokinetics among dogs can be highly variable. Peak is 4-14 hours in dogs and 5-7 hours in cats, with a duration of 6-28 hours in dogs and 13-24 hours in cats. PZI insulin of animal origin (90% bovine and 10% porcine) has been unavailable, but the human recombinant PZI form of insulin has been shown in canine studies to be an effective alternative.
7. **Glargine insulin (Lantus):** A human insulin analogue made from recombinant technology. It has four amino acid differences from feline insulin. It has a slow onset of 4-18 hours and a duration of 24 hours or greater. This analogue is produced by the substitution of glycine for asparagine and the addition of two arginine molecules. These changes shift the isoelectric point toward neutral. In the pH of the vial, it is soluble, but it has reduced solubility at the pH of SQ tissue (microprecipitates), which causes it to be released slowly from the injection site, without a peak. It produces consistent concentrations without large fluctuations in peak and trough seen with other insulin formulations. The glucose-lowering properties are shorter in cats than in people, with a peak at 5-16 hours and duration of 11-24 hours. However, it produces greater glycemic control in cats than other insulins. Remission rates are highest with glargine insulin in cats. Despite the long-lasting effect, optimum control is achieved with twice-daily dosing in cats with glargine insulin. Ordinarily, it is 100 units/mL concentration (Lantus), but there is also a more concentrated form (Toujeo) used in people that is 300 units/mL. The more concentrated form has not been evaluated for pets.

8. **Insulin detemir (Levemir):** 100 units/mL. Long-acting insulin. Insulin detemir has a 14-carbon fatty acid chain which is added by acetylation to lysine, decreases absorption, and is highly bound to albumin. High affinity to albumin in the subcutaneous space prolongs absorption. In cats, the time to onset is approximately 2 hours, time to peak is 7 hours, and duration is 13-14 hours. In dogs, the dose and interval are similar as for glargine insulin. In dogs, it is more potent than other forms, requiring lower doses. A once per 12 hour dose in dogs has provided good regulation.
9. **Insulin glulisine (Apidra), insulin lispro (Humalog), and insulin aspart (NovoLog):** Rapidly acting insulins used in people. They are used for their rapid onset and short duration of action. In people, they are typically used with a meal and combined with a longer-acting form. These rapid-acting insulin analogues have not been evaluated for animals.

## Indications and Clinical Uses

Insulin in its various forms is used to treat diabetes mellitus in dogs and cats. It is used to replace insulin that is deficient. In some cats (approximately 50%), some oral hypoglycemic drugs have been used to reduce use of insulin. However, diabetic dogs are more insulin dependent. Regular insulin is short acting and more useful for emergencies such as diabetic ketoacidosis or acute nonketotic syndromes.

Intermediate or long-acting insulin preparations are used for maintenance and are available in a variety of forms (see previous section). Most of the animal sources of insulin (beef and pork) have been discontinued, and human-recombinant insulin formulations have been substituted without differences in efficacy. In cats, glargine insulin has shown better efficacy than other forms and has been associated with a better remission rate. Glargine also has been used to treat diabetic ketoacidosis in cats and shown to be effective when administered IM. In addition to diabetes mellitus, insulin is occasionally used to treat severe cases of hyperkalemia.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are primarily related to overdoses that result in hypoglycemia.

Glargine insulin has a low pH (4) and may sting from injection. Other insulins are more neutral.

### Contraindications and Precautions

Do not use without the ability to monitor glucose in animals because of the risk of hypoglycemia. Mixing regular insulin and insulins containing zinc in the same syringe will prolong absorption of the regular insulin. Do not mix isophane insulin or phosphate-buffered insulin with zinc insulins (lente, ultralente, semilente). Do *not* use insulin products from compounding pharmacies. Studies to evaluate compounded insulin products for pets have shown that they are unreliable.

### Drug Interactions

Administration of corticosteroids (prednisolone, dexamethasone, etc.) will interfere with action of insulin.

## Instructions for Use

Dietary management is essential for optimal glucose control. Feed cats a high-protein, low-carbohydrate diet. Feed dogs a high-fiber, low-fat diet. Doses should be carefully adjusted in each patient depending on response.

For cats with ketoacidosis, an alternative dosing regimen has used 0.2 units/kg of regular insulin IM initially, then 0.1 units/kg IM every hour until the glucose level is less than 300, then 0.25-0.4 units/kg q6h SQ. With most forms of insulin (including

protamine zinc insulin and glargine insulin) in cats, twice-daily dosing usually is required. However, consider once-daily dosing in cats if blood glucose nadir develops 10 hours or longer after administration. Pet owners are instructed to use appropriate syringe types for administration (e.g., U-40 vs. U-100). Many cats, if properly managed, may go into remission and not require lifelong insulin treatment.

### **Patient Monitoring and Laboratory Tests**

Monitor blood glucose, glycosylated hemoglobin, and/or fructosamine concentrations. When treating diabetes, it is desirable to maintain glucose concentrations between 100 and 300 mg/dL, with the nadir (lowest point) being 80-150 mg/dL.

Serum fructosamine concentrations also can be monitored with the following guidance: <350  $\mu\text{mol/L}$  excellent control, or remission;  $\leq 450$   $\mu\text{mol/L}$  good control; 450-500  $\mu\text{mol/L}$  moderate control; >500  $\mu\text{mol/L}$  poor control.

### **Formulations**

- *See descriptions in “Pharmacology and Mechanism of Action” section.* Human insulin products are usually available in 100 units/mL injection (U-100), with some veterinary products available in smaller concentration of 40 units/mL (U-40, e.g., ProZinc or Vetsulin). Protamine zinc beef-pork (PZI VET) insulin also may be available as 40 units/mL injection (U-40). Some previously available insulin products have been discontinued, such as Iletin II Pork Insulin (regular and NPH formulations), Humulin U Ultralente, and Humulin L Lente (Humulin U and Humulin L).

### **Stability and Storage**

Proper storage is critical for proper action of insulin: keep refrigerated. Warm gently and roll vial prior to injection to ensure proper mixing of vial contents. Do *not* freeze vials of insulin. Do *not* allow vials of insulin to be exposed to heat. Do not mix types of insulin in the same vial or syringe. Veterinarians should not use formulations of insulin that are compounded in unreliable conditions. Dilution of insulin should only be done by a pharmacist because specific diluents must be used.

### **Small Animal Dosage**

#### **Dogs**

- Short-acting regular insulin. Treatment of ketoacidosis for dogs 3 kg: 1 unit/animal initially, then 1 unit/animal q1h; for dogs 3-10 kg: 2 units/animal initially, then 1 unit/animal q1h; and for dogs >10 kg: 0.25 unit/kg initially, then 0.1 unit/kg q1h IM.
- NPH for dogs <15 kg: 1 unit/kg q12-24h SQ (adjust dose with monitoring); dogs >25 kg: 0.5 unit/kg q12-24h SQ (adjust dose with monitoring).
- Vetsulin: Initial dose 0.5 unit/kg, once or twice daily, SQ. Adjust dose (increase or decrease of 25% of dose) by monitoring.
- PZI human recombinant: Can be used as an alternative to beef/pork PZI insulin. Start with 0.5 units/kg, SQ q12h. Median dose in well-controlled dogs is 0.9 units/kg (range 0.4-1.5 units/kg) SQ q12h.
- Glargine insulin: Start with 0.3 units/kg SC q12h. Then monitor glucose to adjust dose. The dose range in well-regulated dogs is 0.32-0.67 units/kg q12h SQ.
- Detemir insulin: 0.12 units/kg, SQ, q12h, (adjust dose as needed). Because of small dose in dogs, a specific diluent may be needed to obtain accurate dose in small dogs.

#### **Cats**

- Short-acting regular insulin. Treatment of ketoacidosis: 0.2 unit/kg IM initially, then 0.1 unit/kg IM every hour until glucose level is less than 300 mg/dL and then continue with 0.25-0.4 unit/kg SQ q6h.

- NPH not recommended for cats, but has been used at 0.25 units/kg SQ q12h, or 1-3 units per cat SQ q12h.
- Protamine zinc recombinant human insulin (ProZinc): Start with 0.2-0.7 units/kg every 12 hours SQ. Adjust dose to achieve nadir of glucose of 80-150 mg/dL.
- PZI insulin: Initial dose is 0.5 unit/kg SQ and then once or twice daily (usually twice is needed) with subsequent doses adjusted to produce desirable glucose levels, usually no higher than 3 units per cat. Final adjusted dose for most cats is 0.9 ( $\pm$  0.4) unit/kg.
- Glargine insulin: Start with 0.5 unit/kg q12h SQ. Some cats can be managed with once-daily dosing, but twice daily is preferred. Adjust dose via monitoring. If treating diabetic ketoacidosis, one may start with glargine insulin administered intramuscularly, then switch to SQ injections for maintenance.
- Detemir insulin: Use same dosage regimen as for glargine insulin.

### Regulatory Information

No regulatory information is available for animals intended for food. Because of low risk of residues, no withdrawal times are suggested.

## Interferon

in-ter-feer'on

**Trade and other names:** Virbagen omega

**Functional classification:** Immunostimulant

### Pharmacology and Mechanism of Action

Recombinant omega interferon contained in Virbagen omega is produced by silkworms previously inoculated with interferon-recombinant baculovirus. It allows the production of pure interferon. Omega interferon of feline origin, produced by genetic engineering, is a type 1 interferon closely related to alpha interferon. The exact mechanism of action of interferon omega is not understood, but it may enhance nonspecific immune defenses in dogs and cats. Interferon does not act directly and specifically on the pathogenic virus, but exerts its effect by inhibition of the internal synthesis mechanisms of the infected cells. After injection, it is bound to receptors in cells infected by the virus, and has a half-life of 1.4 hours in dogs and 1.7 hours in cats.

Multiple interferons are available for human use (e.g., treatment of AIDS-related diseases and cancer-associated diseases). These interferons may be alpha-2a, alpha-2b, n-1, and n-3. These types of interferons are not interchangeable.

### Indications and Clinical Uses

Interferon is used to stimulate the immune system in patients. It has been used to stimulate immune cells in dogs with parvovirus and in cats with feline retrovirus (feline leukemia virus [FeLV] and feline immunodeficiency virus [FIV]). It has not been effective for feline infectious peritonitis (FIP) in cats. It has not been effective for naturally infected FeLV in cats, but has been effective in experimentally infected animals. Human interferon alpha, given orally, has improved clinical signs in cats with FIV.

**Precautionary Information****Adverse Reactions and Side Effects**

Interferon may induce vomiting and nausea. In some animals, it may induce hyperthermia 3-6 hours after injection. In cats, it may produce soft feces to mild diarrhea. A slight decrease in white blood cells, platelets, and red blood cells and an increase in the concentration of ALT may be observed. These parameters usually return to normal in the week following the last injection. In cats, it may induce transient fatigue during treatment.

In people, injections of interferon alpha have been associated with influenza-like symptoms. Other effects, such as bone marrow suppression, also have been reported in people.

**Contraindications and Precautions**

Do not vaccinate dogs or cats receiving interferon.

**Drug Interactions**

Do not mix with any other vaccine/immunologic product, except the solvent supplied for use with the product.

**Instructions for Use**

Doses and indications for animals have primarily been based on extrapolation of human recommendations, experimental studies, or specific studies in cats with viral infections.

**Patient Monitoring and Laboratory Tests**

Monitor complete blood count (CBC) during treatment.

**Formulations Available**

- Interferon is available in 5- and 10-million units/vial. The freeze-dried fraction must be reconstituted with 1 mL of the specific diluent to obtain, depending on the presentation, a solution containing 5 million units or 10 million units of recombinant interferon.

**Stability and Storage**

Interferon has a shelf life of 2 years. The product should be used immediately after reconstitution and should be stored in its original carton. Store and transport at 4° C ± 2° C. Do not freeze.

**Small Animal Dosage****Dogs**

- 2.5 million units/kg IV once daily for 3 consecutive days.

**Cats**

- 1 million units/kg IV or SQ once daily for 5 consecutive days. Three separate 5-day treatments must be performed at day 0, day 14, and day 60.
- 10 units/kg human interferon alpha on an alternate-week schedule PO. (Although oral products may not be absorbed, but some efficacy has been demonstrated from this route.)

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

Do not administer to animals intended for food.

## Iodide (Potassium Iodide)

eye'-oh-dyde

**Trade and other names:** Potassium iodide, EDDI, ethylenediamine dihydriodide

**Functional classification:** Iodine supplement

### Pharmacology and Mechanism of Action

Iodide is administered as a supplement. Although its action for treating disease is not well established, it is administered as an adjunctive treatment for zygomycosis, conidiobolomycosis, and fungal granuloma. The mechanism of action against fungal organisms is not known. Iodide is also important for thyroid gland function and has been used to treat some thyroid disorders.

### Indications and Clinical Uses

Ethylenediamine dihydriodide is used as a nutritional source of iodine in cattle. In people, iodide has been used to treat hyperthyroidism, but effectiveness for this use in cats has not been established. Potassium iodide is also used to protect the thyroid gland from radiation injury in the event of a radiation emergency (accidental exposure to radiation) or following administration of radioactive iodide. Because it may increase respiratory secretions, it has been used as an expectorant, but the efficacy has not been established. Nevertheless in cattle, in addition to a feed supplement, EDDI is used as an expectorant and as an aid in the treatment of bovine infertility. EDDI is sometimes added to the feed of cattle for the purpose of decreasing foot rot infections, lumpy jaw (*Actinomyces bovis*), woody tongue (*Actinobacillus lignieresii*), and bronchitis. There is a lack of published scientific evidence for a beneficial effect. Iodide has been used to treat fungal granulomatous disease and infections associated with zygomycetes. The antifungal treatment has been questioned for animals because the efficacy is not established in horses, iodine is used to treat sporotrichosis and occasionally other fungal infections such as basidiobolomycosis and conidiobolomycosis (zygomycosis). For horses, treatment is initiated with doses listed in the dosing section, and to prevent relapse, treatment is continued for 4 weeks beyond resolution of clinical signs.

In cats, potassium iodide (administered as oral capsules) has been used to treat infections caused by *Sporothrix schenckii*.

### Precautionary Information

#### Adverse Reactions and Side Effects

Iodide-related adverse reactions (iodism) include excess lacrimation, swelling of eyelids, nonproductive cough, increased respiratory secretions, and dermatitis. Its use may cause abortion in horses or limb deformities in foals. Adverse effects are common when used for long periods in small animals. These effects include hepatotoxicity, lethargy, anorexia (most common), vomiting, diarrhea, hypothermia, and cardiomyopathy.

#### Contraindications and Precautions

Do not use in pregnant animals.

#### Drug Interactions

No drug interactions have been reported for small animals.

### Instructions for Use

Iodide has been administered as a 1-g/mL potassium iodine solution (SSKI) or as a 65-mg/mL solution. It also has been administered as a 10% potassium iodide/5% iodine solution given orally with food.

In cattle, EDDI is administered in the feed or mixed with feed, salt, or mineral mixture or in the drinking water.

### Patient Monitoring and Laboratory Tests

Monitor serum thyroid concentrations with prolonged use.

### Formulations

- Available for food animals as EDDI: equivalent to 4.6% EDDI or 46 mg/g of EDDI. Also available as potassium iodide as 1 g/mL potassium iodide solution (SSKI) or a 65-mg/mL oral solution or 10% potassium iodide/5% iodine solution. Inorganic potassium iodide has been used in horses orally, but must be obtained as the chemical grade and compounded for horses.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze solutions. Inorganic potassium iodide is unstable in light, heat, and excess humidity.

### Small Animal Dosage

#### Dogs and Cats

- Fungal infections: Start with 5 mg/kg q8h PO and increase gradually to 25 mg/kg q8h PO.
- Treatment of *Sporothrix* in cats: 15 mg/kg per day oral for 20 weeks.
- Emergency treatment after radiation exposure: 2 mg/kg PO per day.
- Expectorant: 5 mg/kg q8h PO.

### Large Animal Dosage

#### Cattle

- Feed supplement: 50-217 mg EDDI per head per day (mix with feed).
- Expectorant and other indications: 650-1300 mg EDDI per head twice daily PO for 7 days.

#### Horses (Treatment of Fungal Granuloma)

- 20-40 mg/kg per day IV for 7-10 days (using 20% sodium iodide).
- 10-40 mg/kg per day PO (using inorganic potassium iodide).
- 0.86-1.72 mg/kg of EDDI, or use 20-40 mg/kg per day of the 4.6% organic iodine dextrose base of EDDI, PO.

### Regulatory Information

Withdrawal times in food-producing animals have not been established.

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## Ipecac

ih'peh-kak

**Trade and other names:** Ipecac and Syrup of ipecac

**Functional classification:** Emetic

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### Pharmacology and Mechanism of Action

Emetic drug. Ipecac contains two alkaloids: cephalin and emetine. These alkaloids stimulate gastric receptors linked to the chemoreceptor trigger zone (CRTZ) to stimulate vomiting.

## Indications and Clinical Uses

Ipecac is indicated for emergency treatment of poisoning. When used in animals, it should be administered promptly after poisoning. Inducing vomiting with ipecac is not effective beyond 30-60 minutes after poisoning. After successful administration, it is estimated that vomiting removes only 10%-60% of ingested toxicant. Therefore other systemic antidotes and/or activated charcoal should also be considered.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse effects with acute therapy for poisoning. Chronic administration can lead to myocardial toxicity.

#### Contraindications and Precautions

Do not induce vomiting if the patient has ingested caustic chemicals or if there is a risk of aspiration pneumonia.

#### Drug Interactions

Ipecac is not as effective if drugs that act as antiemetics have been administered. Such drugs include tranquilizers (e.g., acepromazine), anticholinergics (e.g., atropine), antihistamines, and prokinetic agents (e.g., metoclopramide).

## Instructions for Use

Ipecac is available as a nonprescription drug. Onset of vomiting may require 20-30 minutes.

## Patient Monitoring and Laboratory Tests

Poisoned animals should be monitored closely because ipecac may not entirely eliminate ingested toxicant.

## Formulations

- Ipecac is available in a 30-mL/bottle oral solution.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 3-6 mL/dog PO. Dose may be increased up to 15 mL per dog for large breeds.

### Cats

- 2-6 mL/cat PO.

## Large Animal Dosage

- Not recommended for large animals.

## Regulatory Information

No regulatory information is available for animals intended for food. Because of low risk of residues, no withdrawal times are suggested.

## Ipodate, Iopanoic Acid

ih'poe-date and i-oh-pa-noe'-ik as-id

**Trade and other names:** Calcium ipodate, Iodopanoic acid

**Functional classification:** Antithyroid agent



## Pharmacology and Mechanism of Action

Cholecystographic agent. This drug is an iodinated biliary radiocontrast dye. Iodate inhibits deiodinases responsible for conversion of thyroid hormone  $T_4$  to  $T_3$ . It also blocks  $T_3$  receptors. It lowers the  $T_3$  level but not the  $T_4$  levels.

## Indications and Clinical Uses

Iodate is used as treatment for hyperthyroidism in cats. Reduction of  $T_3$  levels should occur within 1 week. The use is not as common as other treatments, but it has been administered as an alternative to methimazole, radiation therapy, or surgery. Response rate may be as high as 66%. Iodate formulations may not be available to veterinarians, and iopanoic acid has been used as a substitute. If iopanoic acid (Telepaque) is used as a substitute, it may be less effective.

### Precautionary Information

#### Adverse Reactions and Side Effects

Iodate can cause hypothyroidism. No significant adverse effects have been reported in cats, but compounds containing iodide have caused hypersensitivity reactions in people. In humans, chronic high doses of compounds containing iodide can cause sore mouth, swollen tissues, skin reactions, or GI upset.

#### Contraindications and Precautions

Monitor for reduction of thyroid levels in animals or clinical signs. Relapses have occurred in cats after 10 weeks to 6 months of treatment.

#### Drug Interactions

No drug interactions have been reported for small animals.

## Instructions for Use

Use of iopanoic acid for treatment of hyperthyroidism in cats has been evaluated in small numbers of cats in clinical studies. In one study, most treated cats responded, but it was not considered a long-term treatment. More experience is needed to determine if response to treatment is transient.

## Patient Monitoring and Laboratory Tests

Monitor serum thyroid  $T_3$  concentrations. Iodate lowers the  $T_3$  level, but the  $T_4$  levels may be unchanged or may increase because of decreased conversion of  $T_4$  to  $T_3$ .

## Formulations

- Iodate has been available as either calcium or sodium iodate but some formulations have been discontinued. Oragrafin 500-mg capsules have been formulated into 50-mg capsules by pharmacists. (These may have to be specifically formulated for cats.)

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Cats

- Iodate: 15 mg/kg q12h PO. Most common dose has been 50 mg per cat twice daily. Dose is equivalent regardless of whether sodium or calcium iodate is used.
- Iopanoic acid: 50 mg per cat q12h PO. If adequate response is not observed, increase dose to 100 mg per cat q12h PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Do not administer to animals intended for food.

### Irbesartan

er-beh-sar'tan

**Trade and other names:** Avapro

**Functional classification:** Vasodilator

## Pharmacology and Mechanism of Action

Vasodilator. Angiotensin receptor blocker (ARB). Irbesartan has been shown to block angiotensin II receptors and prevent the effects associated with angiotensin II. It has been used in people who cannot tolerate angiotensin converting enzyme inhibitors (ACE-inhibitors). The metabolism in dogs and cats is uncertain, and it is not known if doses extrapolated from human use have equivalent activity in dogs and cats. Losartan, another ARB, is used as an alternative in people but is reportedly not as effective in dogs because they do not produce the active metabolite.

## Indications and Clinical Uses

Angiotensin II blockers such as irbesartan are used in people as alternatives to ACE inhibitors. However, they are rarely used in animals because most animals tolerate ACE inhibitors well. Use of ARB in animals has been primarily derived from empirical use and studies in which 30 mg/kg was administered to animals with experimentally-induced renal hypertension. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse effects have been reported in animals. Hypotension is a potential problem from overdosing.

#### Contraindications and Precautions

Do not administer to hypotensive or dehydrated animals. No other contraindications have been reported for animals.

#### Drug Interactions

No drug interactions have been reported for small animals. Use cautiously with other vasodilators.

## Instructions for Use

In dogs, irbesartan is preferred over losartan because losartan is not converted to active products in dogs.

## Patient Monitoring and Laboratory Tests

Monitor blood pressure and heart rate in treated animals. Monitor electrolytes if it is administered long term.

## Formulations

- Irbesartan is available in 75-, 150-, and 300-mg tablets. One product (Avalide) contains irbesartan in combination with hydrochlorothiazide.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 30-60 mg/kg q12h PO. Start with 30 mg/kg to avoid prerenal azotemia and hypotension.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI classification: 3

## Iron Dextran, Iron Sucrose

(Note: Oral iron supplements are listed as ferrous sulfate and ferrous gluconate)

**Trade and other names:** AmTech Iron dextran, Ferrodex, and HemaJect. Iron sucrose is Venofer.

**Functional classification:** Mineral supplement

## Pharmacology and Mechanism of Action

Iron supplement. Iron dextran is injected in animals (most commonly pigs) for prevention of iron-deficiency anemia. Iron dextran injection contains either 100 mg elemental iron per mL or 200 mg per mL. Ferric hydroxide is complexed with a low-molecular-weight dextran in this formulation. Iron dextran is a dark brown, slightly viscous liquid complex of ferric oxide and hydrolyzed dextran. After injection, it is slowly absorbed after IM administration into the lymphatic system. It may take 3 weeks for complete absorption. Iron sucrose is injected to treat iron-deficiency anemia.

## Indications and Clinical Uses

Use in animals, primarily young pigs, for treatment and prevention of iron-deficiency anemia. Injections are usually made intramuscularly at 1-4 days of age. Iron dextran also can be administered intramuscularly for treatment of iron deficiency in dogs and cats.

Another preparation is iron sucrose (Venofer) injection 20 mg/mL, which may be used to treat iron-deficiency anemia.

## Precautionary Information

### Adverse Reactions and Side Effects

Injections may produce transient myositis and muscle weakness. The dextran portion can cause anaphylactoid reaction. Use iron sucrose or iron gluconate if the dextran causes a reaction.

### Contraindications and Precautions

When treating patients for iron-deficiency anemia, the total cumulative dose in a 14-day period should not exceed 15 mg/kg. Do not administer solutions intended for IV use by SQ or IM route.

### Drug Interactions

No drug interactions are reported.

## Instructions for Use

Inject iron dextran in midportion of rear thigh muscle in pigs. For treatment of iron-deficiency anemia with iron sucrose, inject intravenously by slow infusion over 2-5 minutes in an undiluted form, or diluted in 100 mL of sodium chloride 0.9% over 15 minutes.

## Patient Monitoring and Laboratory Tests

Monitor iron concentrations in treated animals and CBC to monitor effectiveness. Iron dextran can cause a brown discoloration of serum, with false elevation of bilirubin and false decrease in serum calcium.

## Formulations

- Iron dextran is 100 or 200 milligrams (mg) elemental iron per mL. Iron sucrose is 20 mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, at room temperature, protected from light. Do not mix with other solutions. Do not freeze. When using iron sucrose, use immediately after dilution in saline solutions.

## Small Animal Dosage

- Intravenous use for treating iron-deficiency anemia: 2-3 mg/kg IV slowly over 2-5 minutes. May be repeated five times in a 14-day period. The dose may be diluted in 0.9% saline solution and infused IV.

### Dogs

- 10-20 mg/kg IM of iron dextran once, followed by oral treatment with ferrous sulfate.

### Cats

- 50 mg IM of iron dextran every 3-4 weeks.

## Large Animal Dosage

### Pigs

- 100 mg (1 mL) IM to 2- to 4 day-old pigs; repeat in 10 days.
- 200 mg (1 mL of higher concentration) IM to pigs at 1-3 days of age.

## Regulatory Information

No withdrawal time is necessary.

## Isoflupredone Acetate

eye-soe-floo'preh-done ass'ih-tate

**Trade and other names:** Predef 2X

**Functional classification:** Corticosteroid

## Pharmacology and Mechanism of Action

Corticosteroid. Anti-inflammatory and immunosuppressive effects are approximately 17 times more potent than cortisol and 4 times more potent than prednisolone. Anti-inflammatory effects are complex but primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. Use is for treatment of inflammatory and immune-mediated disease.

## Indications and Clinical Uses

Isoflupredone acetate is used for treating various musculoskeletal, allergic, and systemic inflammatory diseases. Large animal uses include inflammatory disorders, especially musculoskeletal inflammation, and recurrent airway disease (RAO) (formerly called chronic obstructive pulmonary disease [COPD]) in horses. Isoflupredone acetate, like other corticosteroids, has been used to treat ketosis in cattle. In large animals, it also has been used to treat septic shock. However, efficacy for using corticosteroids to treat septic shock is not supported by evidence.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic–pituitary–adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and urinary tract infections (UTIs). In horses, additional adverse effects include risk of laminitis, although a clear association between laminitis and corticosteroids has not been established.

### Contraindications and Precautions

Use with caution in patients prone to infection or GI ulcers. Administration of isoflupredone may induce hepatopathy, diabetes mellitus, or hyperlipidemia. Use cautiously in pregnant animals or in young, rapidly growing animals. Use of corticosteroids may impair healing.

### Drug Interactions

Corticosteroids will increase risk of GI ulceration when administered with NSAIDs.

## Instructions for Use

When administered to treat primary ketosis in cattle, it is advised to also administer IV glucose.

## Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform adrenocorticotrophic (ACTH) stimulation test to monitor adrenal function.

## Formulations

- Isoflupredone is available in a 2-mg injection in 10- and 100-mL vials.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

- No doses are listed for isoflupredone because it is generally not administered to small animals. However, based on anti-inflammatory potency, doses of 0.125–0.25 mg/kg/day IM can be considered.

## Large Animal Dosage

### Cattle

- 10–20 mg total dose per animal q12–24h IM.
- Ketosis: 10–20 mg as a total single dose per animal q12–24h IM.

**Horses**

- 5-20 mg total dose per animal q12-24h IM.
- Pulmonary disease: 0.02-0.03 mg/kg q24h.
- Intraarticular: 5-20 mg per joint.

**Pigs**

- 0.036 mg/kg/day IM.

**Regulatory Information**

Cattle and pig withdrawal time (meat): 7 days.

No milk withdrawal time is listed for US labeling. In Canada, withdrawal times are listed as 5 days for meat and 72 hours for milk.

For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Isoflurane**

eye-soe-floo'rane

**Trade and other names:** Aerrane

**Functional classification:** Anesthetic

**Pharmacology and Mechanism of Action**

Inhalant anesthetic. Like other inhalant anesthetics, the mechanism of action is uncertain. Isoflurane produces a generalized, reversible depression of the central nervous system (CNS). Inhalant anesthetics vary in their solubility in blood, their potency, and the rate of induction and recovery. Those with low blood/gas partition coefficients are associated with the most rapid rates of induction and recovery. Isoflurane has a vapor pressure of 250 mm Hg (at 20° C), a blood/gas partition coefficient of 1.4, and a fat/blood coefficient of 45.

**Indications and Clinical Uses**

Isoflurane, like other inhalant anesthetics, is used for general anesthesia in animals. It is associated with rapid induction of anesthesia and rapid recovery rates. It is metabolized to only a small percent (<1%) and has minimal effects on other organs. It has a minimum alveolar concentration (MAC) value of 1.63%, 1.3%, and 1.31% in cats, dogs, and horses, respectively.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are related to anesthetic effects (e.g., cardiovascular and respiratory depression).

**Contraindications and Precautions**

Do not administer unless it is possible to control ventilation and monitor heart rate and rhythm.

**Drug Interactions**

No drug interactions are reported. However, like other inhalant anesthetics, other anesthetic agents act synergistically and will lower dose requirement.

## Instructions for Use

Use of inhalant anesthetics requires careful monitoring. Dose is determined by depth of anesthesia.

## Patient Monitoring and Laboratory Tests

Monitor respiratory rate, heart rate, and rhythm during administration.

## Formulations

- Isoflurane is available in a 100-mL bottle.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

- Induction: 5%; maintenance: 1.5%-2.5%.

## Large Animal Dosage

- MAC value: 1.5%-2%.

## Regulatory Information

Withdrawal times are not established for animals that produce food. Clearance is rapid, and short withdrawal times are suggested.

For extralabel use with withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Isoniazid

eye-soe-nye'-a-zid

**Trade and other names:** INH, Isonicotinic acid hydrazide

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Antibacterial agent. Mechanism of action is via interference with lipid and nucleic acid biosynthesis in actively growing tubercle bacilli.

## Indications and Clinical Uses

Isoniazid is used in people to treat tuberculosis. In animals, it is used to treat atypical bacterial infections, such as those caused by *Mycobacterium*.

## Precautionary Information

### Adverse Reactions and Side Effects

The use is uncommon in animals, and adverse effects have not been well documented. Hepatic toxicity is the most serious concern when isoniazid is used in people, which is apparently caused by a metabolite and may have a delayed onset. Other reported adverse effects include rash and peripheral neuropathy.

### Contraindications and Precautions

No specific contraindications have been reported for animals. However, it should not be used in animals with evidence of hepatic disease.

### Drug Interactions

Isoniazid metabolism may be decreased by itraconazole and increased by rifampin.

## Instructions for Use

Isoniazid administration in animals is limited to indications where other drugs are not effective.

## Patient Monitoring and Laboratory Tests

Monitor liver enzymes. Monitor patients for signs of neurologic toxicity.

## Formulations

- Isoniazid is available in 100- and 300-mg tablets; 10-mg/mL syrup; or 100-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

- 5 mg/kg per day (up to 10-15 mg/kg/day) PO, IM, or IV. It also is administered as 15 mg/kg two to three times per week.

## Large Animal Dosage

- No dose reported.

## Regulatory Information

No withdrawal time has been established for large animals. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Isoproterenol Hydrochloride

eye-soe-proe-teer'eh-nole hye-droe-klor'idē

**Trade and other names:** Isuprel and Isoprenaline hydrochloride

**Functional classification:** Beta-agonist

## Pharmacology and Mechanism of Action

Adrenergic agonist. Isoproterenol stimulates both  $\beta_1$ - and  $\beta_2$ -adrenergic receptors, with little effect on  $\alpha$ -receptors. Like other beta-agonists, it stimulates activity of adenylyl cyclase. In cardiac tissue, isoproterenol is one of the most potent agonists and will increase rate, conduction, and contractility. Beta-agonists will also relax bronchial smooth muscle and arterial smooth muscle. It has a rapid onset of activity, with rapid systemic clearance and short duration of action.

## Indications and Clinical Uses

Isoproterenol is administered when it is necessary for prompt stimulation of the heart (inotropic and chronotropic) or to relieve acute bronchoconstriction. It is short acting and must be administered by IV or via inhalation.

## Precautionary Information

### Adverse Reactions and Side Effects

Isoproterenol causes adverse effects related to excessive adrenergic stimulation, seen primarily as tachycardia and tachyarrhythmias. High doses can cause calcium accumulation in myocardium and tissue injury. Adrenergic agonists can produce potassium imbalance in animals.



**Contraindications and Precautions**

Do not use if formulation turns pink or a dark color.

**Drug Interactions**

Isoproterenol will potentiate other adrenergic agonists. Treatment will potentiate cardiac arrhythmias and should be used cautiously with other arrhythmogenic drugs.

**Instructions for Use**

Because of a short half-life, isoproterenol must be infused via constant-rate infusion (CRI) or repeated if administered IM or SQ. It is recommended for short-term use only because repeated treatment will cause cardiac injury.

**Patient Monitoring and Laboratory Tests**

Monitor heart rate and rhythm during treatment. Monitor serum potassium with repeated use.

**Formulations**

- Isoproterenol is available in 0.2-mg/mL ampules for injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water with good aqueous stability. It is susceptible to light, and if a dark color is observed, it should be discarded (pink to brownish color). Solutions above pH 6.0 may decompose more rapidly. In 5% dextrose solutions, it is stable for 24 hours. It has been added to ultrasonic nebulizers in distilled water for respiratory therapy and was stable in solution for 24 hours. It also is stable if mixed with cromolyn sodium.

**Small Animal Dosage****Dogs and Cats**

- 10 mcg/kg q6h IM or SQ.
- Dilute 1 mg in 500 mL of 5% dextrose or lactated Ringer's solution and infuse IV 0.5-1 mL/min (1-2 mcg/min) or to effect.
- CRI: Administer to effect at 0.01-0.1 mcg/kg/min.

**Large Animal Dosage**

- 1 mcg/kg q15min IV until desired response.

**Regulatory Information**

No regulatory information is available for animals intended for food. Because of low risk of residues, no withdrawal times are suggested.

RCI classification: 2

**Isosorbide Dinitrate, Isosorbide Mononitrate**

eye-soe-sor'bide dye-nye'trate, eye-soe-sor'bide mahn-oh-neye'trate

**Trade and other names:** Isosorbide dinitrate: Isordil, and Isosorbide mononitrate: Monoket

**Functional classification:** Vasodilator

## Pharmacology and Mechanism of Action

Nitrate vasodilator. Like other nitrovasodilators, it produces vasodilation via generation of nitric oxide. It relaxes vascular smooth muscle, especially venous vessels. Consequently, it decreases atrial pressure, as well as afterload and preload. Isosorbide mononitrate is a biologically active form of isosorbide dinitrate. Compared to isosorbide dinitrate, it does not undergo first-pass metabolism and is completely absorbed orally.

## Indications and Clinical Uses

Isosorbide dinitrate is used to reduce preload in patients with congestive heart failure (CHF). In people, it is primarily used to treat angina. The use in animals has not been established, and nitroglycerin is used more frequently (topically) or infusions of nitroprusside IV are used in critical care situations. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are primarily related to overdoses that produce excess vasodilation and hypotension. Tolerance may develop with repeated doses.

#### Contraindications and Precautions

Do not administer to patients with hypovolemia. Use cautiously in animals with low cardiac reserve.

#### Drug Interactions

No drug interactions are reported.

## Instructions for Use

Generally, doses are titrated to individuals depending on response. Isosorbide mononitrate is absorbed better than isosorbide dinitrate and may be preferred in clinical situations.

## Patient Monitoring and Laboratory Tests

Monitor patient's cardiovascular status during treatment.

## Formulations

- Isosorbide dinitrate is available in 5-, 10-, 20-, and 40-mg tablets and 40-mg capsules.
- Isosorbide mononitrate is available in 10- and 20-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- Isosorbide dinitrate: 2.5-5 mg/animal q12h PO or 0.22-1.1 mg/kg q12h PO.
- Isosorbide mononitrate: 5 mg/dog; administer two doses per day 7 hours apart PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

There is a low risk of residue potential.

RCI classification: 4

**Isotretinoin**

eye-soe-tret'ih-noe-in

**Trade and other names:** Accutane, Absorica**Functional classification:** Dermatologic agent**Pharmacology and Mechanism of Action**

Isotretinoin is a keratinization-stabilizing drug. Isotretinoin reduces sebaceous gland size, inhibits sebaceous gland activity, and decreases sebum secretion. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

**Indications and Clinical Uses**

In people, it is primarily used to treat acne. In animals, it has been used to treat sebaceous adenitis.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are not reported for animals, although experimental studies have demonstrated that it can cause focal calcification (such as in myocardium and vessels).

**Contraindications and Precautions**

Isotretinoin is absolutely contraindicated in pregnant animals because of fetal abnormalities.

**Drug Interactions**

No drug interactions are reported.

**Instructions for Use**

Use in veterinary medicine is confined to limited clinical experience and extrapolation from human reports. High expense of this medication has limited veterinary use. There is a restricted distribution for humans and it may not be available for veterinary use.

**Patient Monitoring and Laboratory Tests**

No monitoring is necessary for animal use.

**Formulations**

- Isotretinoin is available in 10-, 20-, and 40-mg capsules. Capsules may not be available for veterinary use.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs**

- 1-3 mg/kg/day (up to a maximum recommended dose of 3-4 mg/kg/day PO).

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

Do not use in animals intended for food.

## Isoxsuprine

eye-soks'yoo-preen

**Trade and other names:** Vasodilan and generic brands

**Functional classification:** Vasodilator

### Pharmacology and Mechanism of Action

Vasodilator. The mechanism of action for isoxsuprine has not been identified. It has been suggested to act as a beta<sub>2</sub>-agonist (for which experimental evidence is not supportive) or by increasing concentrations of nitric oxide. It also may inhibit mechanisms that are calcium dependent. It relaxes vessels in digits of horses.

### Indications and Clinical Uses

Isoxsuprine is used in horses for navicular disease and other diseases of the foot, such as laminitis. The efficacy has not been established for these indications, even though the use has persisted for many years. There are no reports of its use in other animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Hypotension is the primary adverse effect. It lowers arterial pressure. In horses, side effects may also include rubbing noses on objects, hyperexcitability, sweating, tachycardia, and restlessness.

#### Contraindications and Precautions

Do not use in hypotensive or dehydrated animals.

#### Drug Interactions

No drug interactions are reported.

### Instructions for Use

When used in horses, it often is used with other vasodilators and anti-inflammatory drugs. It is not known if it acts synergistically with these other medications.

### Patient Monitoring and Laboratory Tests

Monitor heart rate in treated animals.

### Formulations

- Isoxsuprine is available in 10- and 20-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Although isoxsuprine is compounded for equine use, stability of compounded formulations has not been evaluated.

### Small Animal Dosage

- No small animal doses are reported.

### Large Animal Dosage

#### Horses

- Navicular disease and laminitis: 0.6 mg/kg q12h PO for 6-14 weeks. In some dosing protocols, if 0.6 mg/kg q12h has not improved horse's condition within 3 weeks, the dose has been doubled.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Itraconazole

it-rah-kahn'ah-zole

**Trade and other names:** Sporanox and Itrafungol (available in Europe for cats)

**Functional classification:** Antifungal

## Pharmacology and Mechanism of Action

Azole (triazole) antifungal drug. Itraconazole inhibits ergosterol synthesis in fungal cell membrane. Fungistatic. It is active against dermatophytes and systemic fungi, such as *Blastomyces*, *Histoplasma*, and *Coccidioides*. It is more potent against these fungi than ketoconazole. Itraconazole can be incorporated into sebum and stratum corneum and can be detected in skin for 3-4 weeks after treatment.

Experience in dogs and cats has shown it to be absorbed orally, and doses have been established for treating systemic fungal infections and dermatophytes. In horses, the oral solution is better absorbed than the capsules (65% vs. 12%). The half-life for the solution is 11 hours. In dogs, the approved formulation is absorbed with a peak of 3 hours and a terminal half-life of approximately 7 hours. Peak concentrations in dogs are approximately 1.4 mcg/mL. Human-label generic, but not compounded, formulations produce similar concentrations in dogs. In cats the oral solution is absorbed approximately 5x higher than the oral capsule. After absorption in cats the half-life is approximately 20 hours and every-other-day dosing is possible.

## Indications and Clinical Uses

Itraconazole is used to treat dermatophytes and systemic fungi, such as *Blastomyces*, *Histoplasma*, and *Coccidioides*. It also has been shown effective for treatment of *Malassezia* dermatitis, but doses are lower than for other infections (see [dosing](#) section). Although it has been used to treat infections caused by *Aspergillus* spp., efficacy has not been as good as with other antifungal drugs such as voriconazole or amphotericin B. Itraconazole is often considered the first choice for dermatophyte infections in cats.

## Precautionary Information

### Adverse Reactions and Side Effects

Itraconazole is better tolerated than ketoconazole. Ketoconazole inhibits hormone synthesis and can lower concentrations of cortisol, testosterone, and other hormones in animals. However, itraconazole has little effect on these enzymes and will not produce endocrine effects. However, vomiting and hepatotoxicity are possible, with itraconazole administration, especially at high doses. Approximately 10%-15% of dogs will develop high liver enzyme levels. Itraconazole has produced skin lesions in dogs, consisting of vasculitis, sterile suppurative skin lesions, and ulcerative skin lesions. High doses in cats caused vomiting and anorexia.

### Contraindications and Precautions

Dose with food for best oral absorption. Compounded formulations are not bioequivalent to proprietary forms and should be avoided for use in animals. Use itraconazole cautiously in any animal with signs of liver disease. Use cautiously in pregnant animals. At high doses in laboratory animals, it has caused fetal abnormalities.

### Drug Interactions

Antacid drugs (proton pump inhibitors or H<sub>2</sub>-receptor blockers) will decrease oral absorption. Itraconazole is a cytochrome P450 enzyme inhibitor. It may cause drug interactions because of inhibition of P450 enzymes. The extent of cytochrome P450 inhibition is not as high as for ketoconazole, but may be important for some of the low therapeutic index drugs (see Appendixes H and I).

### Instructions for Use

Administer with food for best absorption, unless the oral solution is used. Doses are based on studies in animals in which itraconazole has been used to treat blastomycosis in dogs (median dose 5.5 mg/kg per day). Lower doses may be used in cats and dogs for dermatophytes and in dogs for treating *Malassezia* dermatitis. Doses in horses are based on specific pharmacokinetic studies. Other uses or doses are based on empiricism or extrapolation from human literature.

Ordinarily, oral formulations are administered. However, it may be administered intravenously if needed. If IV solutions are used, infuse over 30 minutes.

### Patient Monitoring and Laboratory Tests

Monitor liver enzyme concentrations. If plasma/serum drug concentrations are monitored, the trough concentration (immediately before next dose) should be in the range of 0.5-1 mcg/mL.

### Formulations Available

- Itraconazole is available in 100-mg capsules and 10-mg/mL oral liquid.
- Itrafungol for cats is a 10-mg/mL oral liquid (available in Europe). Injection form (if available) is 10 mg/mL supplied in 25-mL ampules (250 mg).

### Stability and Storage

Itraconazole is practically insoluble in water, but is soluble in ethanol. It is unstable and may lose potency if not maintained in manufacturer's original formulation (capsules and solution). Compounded formulations are highly unstable and insoluble. Oral absorption of compounded itraconazole suspensions and capsules is poor or barely detectable and is not recommended. Oral commercial formulation (in cyclodextran) has a pH of approximately 2.0, and the pH should be maintained to ensure optimal absorption. Do not freeze. The 10-mg/mL injection solution can be reconstituted with saline (but not dextrose or lactated Ringer's solution) and stored at either 2°-8° C or room temperature for up to 48 hours after reconstitution. Do not mix with other drugs.

### Small Animal Dosage

#### Dogs

- 2.5 mg/kg q12h or 5 mg/kg q24h PO. For refractory cases, use 10 mg/kg q12h PO to increase blood concentrations.
- Dermatophytes: 3 mg/kg/day, PO, for 15 days.
- Cryptococcosis: 5 mg/kg q12h PO.
- *Malassezia* dermatitis: 5 mg/kg q24h PO for 2 days, repeated each week for 3 weeks.

#### Cats

- 5 mg/kg PO once daily. Alternatively, 50 mg (total dose) once per day; or 100 mg per cat once every other day.
- Dermatophytes: 1.5-3 mg/kg (up to 5 mg/kg) q24h PO for 15 days (although some cats needed an additional 15-day course of therapy).
- 5-10 mg/kg q24h PO for 7 days, then alternating with 1 week on and 1 week off.

## Large Animal Dosage

### Horses

- 5 mg/kg/day (2.5 mg/kg q12h) PO. In horses, the capsules are absorbed poorly and inconsistently. Use the oral solution (Sporanox) for optimum oral absorption.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Ivermectin

eye-ver-mek'tin

**Trade and other names:** Heartgard, Ivomec, Eqvalan liquid, Equimectrin, IverEase, Zimecterin, Privermectin, Ultramectin, Ivercide, Ivercare, and Ivermax. Acarexx is a topical form for cats.

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Antiparasitic drug. Avermectins (ivermectin-like drugs) and milbemycins (milbemycin and moxidectin) are macrocyclic lactones and share similarities, including mechanism of action. These drugs are neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Paralysis and death of the parasite are caused by increased permeability to chloride ions and hyperpolarization of nerve cells. These drugs also potentiate other chloride channels, including ones gated by gamma-aminobutyric acid (GABA). Mammals ordinarily are not affected because they lack glutamate-gated chloride channels, and there is a lower affinity for other mammalian chloride channels. Because these drugs ordinarily do not penetrate the blood-brain barrier, GABA-gated channels in the CNS of mammals are not affected. Ivermectin is active against intestinal parasites, mites, bots, heartworm microfilaria, and developing larvae. Ivermectin can also produce heartworm adulticide effects when administered long term. Ivermectin has no effect on trematode or cestode parasites.

After SQ injection in dogs, the half-life was slow (100-145 hours) and absorption was slow.

## Indications and Clinical Uses

Ivermectin is used in horses for the treatment and control of large strongyles (adult) (*Strongylus vulgaris*, *S. edentatus*, and *Triodontophorus* species), small strongyles (adult and fourth-stage larvae) (*Cyathostomum* spp., *Cylicocyclus* spp., *Cylicostephanus* spp.), pinworms (adult and fourth-stage larvae) (*Oxyuris equi*), large roundworms (adult) (*Parascaris equorum*), hairworms (adult) (*Trichostrongylus axei*), large-mouth stomach worms (adult) (*Habronema muscae*), neck threadworms (microfilariae) (*Onchocerca* spp.), and stomach bots (*Gastrophilus* spp.). In cattle, it is used for treatment and control of GI nematodes (adults and fourth-stage larvae) (*Haemonchus placei*, *Ostertagia ostertagi*) (including inhibited larvae), *O. lyrata*, *T. axei*, *T. colubriformis*, *Cooperia oncophora*, *C. punctata*, *C. pectinata*, *Oesophagostomum radiatum*, *Nematodirus helvetianus* (adults only), *N. spathiger* (adults only), *Bunostomum phlebotomum*; lungworms (adults and fourth-stage larvae) (*Dictyocaulus viviparus*); grubs (parasitic stages) (*Hypoderma bovis*, *H. lineatum*); sucking lice (*Linognathus vituli*, *Haematopinus eurysternus*, *Solenopotes capillatus*); and mites (scabies) (*Psoroptes ovis* [syn. *P. communis* var. *bovis*], *Sarcoptes scabiei* var. *bovis*).

In pigs, it is used for treatment and control of GI roundworms (adults and fourth-stage larvae) (large roundworm, *Ascaris suum*; red stomach worm, *Hyostrogylus rubidus*; nodular worm, *Oesophagostomum* species; threadworm, *Strongyloides ransomi* (adults only); somatic roundworm larvae (threadworm, *S. ransomi* [somatic larvae]); lungworms (*Metastrongylus* spp. [adults only]); lice (*H. suis*); and mites (*Sarcoptes scabiei* var. *suis*).

In small animals (dogs and cats), it is used as a heartworm preventative (low dose) or to treat external parasites (mites) and intestinal parasites at higher doses. The benefit for heartworm prophylaxis in animals is the ability to kill young larvae, older larvae, and immature or young adults and adult filariae. Ivermectin is an effective microfilaricide after adulticide therapy. It has been recommended by the American Heartworm Society to treat heartworm-positive dogs for 2-3 months prior to adulticide therapy. This allows immature worms to reach full maturity that are more susceptible to melarsomine, as well as preventing new infection. Ivermectin can also reduce numbers of adult heartworms when administered long term at preventive doses. For optimal heartworm adulticide effect, it is often administered with oral doxycycline (10 mg/kg per day) for several months. Treatment of *Demodex* infections is effective but requires higher doses than for any other indication.

## Precautionary Information

### Adverse Reactions and Side Effects

Toxicity may occur at high doses and in breeds in which ivermectin crosses the blood-brain barrier. Sensitive breeds include collies, Australian shepherds, Old English sheepdogs, longhaired whippets, and Shetland sheepdogs. Toxicity is neurotoxic and signs include hypersalivation, depression, ataxia, difficulty with vision, coma, and death. Sensitivity to ivermectin occurs in certain breeds because of a mutation in the multidrug resistance gene (ABCB1, formerly MDR1 gene) that codes for the membrane pump P-glycoprotein (P-gp). This mutation affects the efflux pump in the blood-brain barrier. Therefore ivermectin can accumulate in the brain of susceptible animals. High doses in normal animals may also produce similar toxicosis. Most nonsusceptible dogs can tolerate doses of 100-400 mcg/kg. But sensitive breeds (dogs with the ABCB1 mutation) may exhibit toxicity at doses of 150-340 mcg/kg. Retinopathy has also been observed in dogs administered high doses. In affected animals, a sudden onset of blindness and/or mydriasis may occur, but dogs recover if the drug is discontinued. Ivermectin at doses of 400 mcg/kg has produced neurological toxicosis in Siamese kittens, and doses as low as 300 mcg/kg have been lethal in kittens. In horses, adverse reactions may include itching because of effects on microfilariae.

### Contraindications and Precautions

Do not administer to animals younger than 6 weeks of age. Animals with high numbers of microfilaremia may show adverse reactions to high doses. If dogs are sensitive to ivermectin (see earlier list of breeds), they may be sensitive to other drugs in this class (avermectins). Ivermectin at approved clinical doses for treatment of endoparasites or heartworm prevention has been safe in pregnant animals. At high doses used for treating demodicosis, safety during pregnancy is not known, but there have been no reports of teratogenic effects. In the most sensitive laboratory animal (mouse), the lowest dose that is teratogenic is 400 mcg/kg. Dogs with the ABCB1 (MDR) mutation may also be sensitive to other drugs such as loperamide, milbemycin, moxidectin, and anticancer drugs. Ivermectin is excreted in milk.



### Drug Interactions

Do not administer with drugs that could potentially increase the penetration of ivermectin across the blood-brain barrier. Such drugs include ketoconazole, itraconazole, cyclosporine, and calcium-channel blockers.

### Instructions for Use

Ivermectin is used in a wide range of animals for internal and external parasites. Dosage regimens vary, depending on the species and parasite treated. Heartworm prevention is the lowest dose; other parasites require higher doses. Products for heartworm prevention and a topical form are the only forms approved for small animals; for other indications, large-animal injectable products are often administered PO, IM, or SQ to small animals. Do not administer intravenously. Injections in pigs should be made in the neck only. Because some dogs may be sensitive to ivermectin, if a dog has not previously received ivermectin and high doses are needed (e.g., to treat *Demodex*), start with a low dose (50-100 mcg/kg), then increase by increments of 50-100 mcg/kg/day on subsequent doses every day. During this increase, the dog should be observed for signs of CNS toxicity (ataxia, tremors, sedation). Once the maintenance dose is achieved (300-600 mcg/kg, PO), it should be administered once daily until 4 weeks after the second consecutive negative monthly skin scraping. When using extralabel formulations to treat dogs, the aqueous formulations have better palatability than the propylene-based formulations.

### Patient Monitoring and Laboratory Tests

Monitor for microfilaremia prior to administration in small animals. For other parasitic infections, confirm successful treatment with fecal examinations or skin scrapings.

### Formulations

- Ivermectin is available in 1% (10 mg/mL), 2% (20 mg/mL), and 0.27% (2.7 mg/mL) injectable solution; 10-mg/mL oral solution; 0.8-mg/mL oral sheep drench; 18.7-mg/mL oral paste; 68-, 136-, and 272-mcg tablets; and 55- and 165-mg feline tablets. A water-soluble topical product 0.01% (0.1 mg/mL) is available in ampules in foil pouches for treating ear mites in cats.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- Heartworm preventative: 6 mcg/kg q30day PO.
- Prior to adulticide treatment: Administer preventative dose for up to 3 months prior to adulticide treatment.
- Microfilaricide: 50 mcg/kg PO 2 weeks after adulticide therapy.
- Heartworm adulticide: Ivermectin administered at preventive doses combined with doxycycline at 10 mg/kg PO per day periodically (4 weeks at a time) for several months.
- Ectoparasite therapy: 200-400 mcg/kg (0.2-0.4 mg/kg) IM, SQ, or PO.
- Demodicosis therapy: Start with 100 mcg/kg/day (0.1 mg/kg) and increase dose by 100 mcg/kg/day to 600 mcg/kg/day (0.6 mg/kg) for 60-120 days PO. (Successful treatment is confirmed with negative skin scrapings.)
- Sarcoptic mange and Cheyletiellosis therapy: 200-400 mcg/kg q7days PO or q14 days SQ for 4-6 weeks.

**Cats**

- Heartworm preventative: 24 mcg/kg q30 days PO.
- Ectoparasite therapy: 200-400 mcg/kg (0.2-0.4 mg/kg) IM, SQ, or PO, every 7 days, or as needed based on skin scraping and clinical examination.
- Endoparasite therapy: 200-400 mcg/kg (0.2-0.4 mg/kg) weekly SQ or PO.
- Topical: 0.5 mL per ear (0.1 mg/mL) for treating ear mites.

**Large Animal Dosage****Horses**

- 200 mcg/kg (0.2 mg/kg) IM, oral paste, or oral solution. Administer once, or as needed as part of a comprehensive worming program.

**Calves**

- Slow-release bolus: 5.7-13.8 mg/kg, as a single dose, which has a duration of 135 days.

**Cattle and Goats**

- Injection solution: 200 mcg (0.2 mg)/kg as a single dose SQ.

**Pigs**

- 300 mcg (0.3 mg)/kg SQ as a single dose.

**Sheep**

- Injection solution: 200 mcg (0.2 mg)/kg as a single dose SQ.
- 200 mcg/kg PO.

**Regulatory Information**

Pigs' withdrawal time for meat: 18 days for SQ injection.

Cattle and calves withdrawal time (meat): 35 days for SQ injection or 180 days for slow-release bolus. Forty-eight days for topical (pour-on).

Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.

Sheep withdrawal time (meat): 11 days.

Goats' withdrawal time: 11-14 days (meat) and 6-9 hours (milk). When administering SQ to goats, use 35 hours for meat and 40 hours for milk.

**Ivermectin + Praziquantel**

eye-ver-mek'tin + pray-zih-kwon'tel

**Trade and other names:** Equimax

**Functional classification:** Antiparasitic

**Pharmacology and Mechanism of Action**

Antiparasitic drug. Ivermectin + praziquantel is indicated for use in horses for treatment and control of tapeworms, large strongyles (including *Strongylus vulgaris*, *S. edentatus*, *S. equines*) and small strongyles, pinworms, ascarids, hairworms, stomach worms, bots, *Habronema* spp., and other parasites.

**Indications and Clinical Uses**

Ivermectin has properties as described in the Ivermectin monograph. Praziquantel is added to this formulation to increase the spectrum.

### Precautionary Information

#### Adverse Reactions and Side Effects

Toxicity may occur at high doses. Ivermectin appears to be safe for pregnant animals.

#### Contraindications and Precautions

Ivermectin can be administered to breeding, pregnant, and lactating animals without adverse effects.

#### Drug Interactions

Use cautiously with other drugs that may affect penetration across the blood–brain barrier.

### Instructions for Use

Use of this drug is similar to the individual drugs ivermectin and praziquantel.

### Patient Monitoring and Laboratory Tests

Fecal samples should be examined for parasites to monitor effectiveness.

### Formulations

- Ivermectin + praziquantel is available in a paste composed of 1.87% ivermectin and 14.03% praziquantel.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

- No dose available for small animals.

### Large Animal Dosage

#### Horses

- 200 mcg/kg ivermectin and 1 mg/kg praziquantel PO.

### Regulatory Information

No withdrawal times are available for animals intended for food (extralabel use).

## Kanamycin Sulfate

kan-ah-mye'sin sul'fate

**Trade and other names:** Kantrim

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Aminoglycoside antibiotic. Bactericidal. Like other aminoglycosides, kanamycin acts to inhibit bacteria protein synthesis via binding to the 30S ribosome. Kanamycin has a broad spectrum of activity that includes *Staphylococcus* spp. and gram-negative bacilli. It has weak activity against streptococci and anaerobic bacteria. Kanamycin is not as active against most bacteria as gentamicin or amikacin.

### Indications and Clinical Uses

Kanamycin is a broad-spectrum antibiotic used to treat gram-negative infections. It is less active than gentamicin, amikacin, or tobramycin. Therefore there is little advantage for using kanamycin over the other drugs in this class. The use of kanamycin has greatly diminished and gentamicin and amikacin are much more frequently used in animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Nephrotoxicity is the most dose-limiting toxicity. Ensure that patients have adequate fluid and electrolyte balance during therapy. Ototoxicity and vestibulotoxicity also are possible.

#### Contraindications and Precautions

Do not use in animals with renal disease. Do not use in dehydrated animals.

#### Drug Interactions

When used with anesthetic agents, neuromuscular blockade is possible with high doses. Do not mix in vial or syringe with other antibiotics. Ototoxicity and nephrotoxicity are potentiated by loop diuretics such as furosemide.

### Instructions for Use

Kanamycin is not as active as other aminoglycosides. For serious infections, consider gentamicin or amikacin.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) minimum inhibitory concentration (MIC) value break point for susceptibility is less than or equal to 16 mcg/mL. Monitor blood urea nitrogen (BUN), creatinine, and urine for evidence of renal toxicity.

### Formulations

- Kanamycin is available in 200- and 500-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water but is not stable in compounded formulations. Do not mix with other drugs. Do not freeze.

## Small Animal Dosage

### Dogs and Cats

- 10 mg/kg q12h IV or IM.
- 20 mg/kg q24h IV or IM.

## Large Animal Dosage

### Horses

- 10 mg/kg q24h IV.

## Regulatory Information

Avoid use in food-producing animals. Extended withdrawal times (as long as 18 months) may be needed for withdrawal time in cattle. For extralabel use with-drawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

## Kaolin and Pectin

kay'oh-lin + pek'tin

**Trade and other names:** Generic brands only

**Functional classification:** Antidiarrheal

## Pharmacology and Mechanism of Action

Antidiarrheal compound. Kaolin is a form of aluminum silicate, and pectin is a carbohydrate that is extracted from the rinds of citrus fruits. This product has a claim to act as a demulcent and adsorbent in the treatment of diarrhea. The action of kaolin-pectin is believed to be related to the binding of bacterial toxins (endotoxins and enterotoxins) in the gastrointestinal (GI) tract. However, experimental studies have shown that kaolin-pectin has been an ineffective binder of *Escherichia coli* enterotoxin, and clinical studies have failed to show a benefit from the administration of kaolin-pectin. This product may change the consistency of stools, but it will not decrease fluid or electrolyte loss, nor will it shorten the duration of illness. Most of the modern Kao-Pectate formulations contain salicylate as one of the active ingredients.

## Indications and Clinical Uses

Kaolin and pectin combinations are used for the symptomatic treatment of acute diarrhea. Despite the lack of clinical evidence of efficacy, some veterinarians administer this drug for short-term treatment. Commercial forms that contain salicylate (8.68 mg/mL) may have anti-inflammatory effects to decrease secretory diarrhea caused by bacteria.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects are uncommon. There is 8.7 mg/mL salicylate in the regular strength and 16 mg/mL in the extra-strength formulation. Because some animals may be sensitive to salicylates, this ingredient in the formulation should be considered before administering to animals.

### Contraindications and Precautions

No specific contraindications in animals.

### Drug Interactions

No drug interactions are reported. However, the kaolin component may prevent absorption of other drugs. Administer other oral drugs 30 minutes prior to kaolin-pectin to avoid drug interaction.

### Instructions for Use

Kaolin-pectin may not change the course of diarrhea, but may change the character of the feces.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Kaolin-pectin is no longer found in the product Kao-Pectate (previously available in a 12-oz. oral suspension). All formulations for Kao-Pectate contain bismuth subsalicylate. Salicylate (8.68 mg/mL) is present in Kao-Pectate.
- Veterinary formulations of kaolin-pectin are available under various generic names in 1-quart and 1-gallon containers containing 5.8 g of kaolin and 0.139 g of pectin per 30 mL (1 ounce).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 1-2 mL/kg q2-6h PO.

### Large Animal Dosage

#### Horses and Cattle

- 180-300 mL q2-3h PO.

#### Calves and Foals

- 90-120 mL q2-3h PO.

### Regulatory Information

There is little risk of residues in animals that produce food. No withdrawal times are necessary.

## Ketamine Hydrochloride

ket'ah-meen hye-droe-klor'ide

**Trade and other names:** Ketalar, Ketavet, and Vetalar

**Functional classification:** Anesthetic

### Pharmacology and Mechanism of Action

Anesthetic agent. Exact mechanism of action is not known, but most evidence supports its action as a centrally acting dissociative agent. Ketamine produces mild analgesia and modulates pain via its ability to act as a noncompetitive antagonist for n-methyl D-aspartate (NMDA) receptors. Ketamine is an equal concentration of two isomers (R-ketamine and S-ketamine). S-ketamine is more active and eliminated faster. Ketamine is rapidly metabolized in most animals (60- to 90-minute half-life in dogs); however, a metabolite (norketamine) may produce more prolonged NMDA antagonistic effects.

## Indications and Clinical Uses

Ketamine is used for short-term anesthetic procedures. Duration of action is generally 30 minutes or less. Ketamine has some analgesic properties via its effects on NMDA receptors and has been administered as an adjunct to other analgesic medications, usually with opiates, sometimes as a slow continuous-rate infusion (CRI). Ketamine is often combined in use with other anesthetics and sedatives such as benzodiazepines (diazepam), propofol, opiates (hydromorphone) or  $\alpha_2$  agonists (medetomidine, dexmedetomidine, and xylazine). Such combinations have been synergistic and allowed lower doses of each individual component. One example of a combination is MLK, which is morphine (or fentanyl), lidocaine, and ketamine (see [dosing](#) section), or equine “triple-drip” in which it is mixed with xylazine and guaifenesin (see [dosing](#) section for more details).

Although ordinarily contraindicated in patients with epilepsy, it has been used to treat cases of refractory status epilepticus through its NMDA receptor effects.

## Precautionary Information

### Adverse Reactions and Side Effects

Ketamine causes pain with IM injection (pH of solution is 3.5). Tremors, muscle spasticity, and convulsive seizures have been reported. Spontaneous movements, salivation, and increased body temperature are more common in dogs when high doses are used. Ketamine will increase heart rate and blood pressure as a result of an increase in sympathetic tone. It will produce an increased cardiac output compared to other anesthetic agents. Salivation, mydriasis, and regurgitation are increased in animals that receive ketamine, which may be reduced by premedication within atropine. Apnea may develop in some animals, and oxygen supplementation should be provided.

### Contraindications and Precautions

Do not use in animals with head injury because it may elevate cerebrospinal fluid (CSF) pressure. Use cautiously, if at all, in animals with glaucoma (increases intraocular pressure). Do not use in animals prone to seizures (although some animals with seizures have been successfully treated with ketamine). When used alone as a sole agent in horses, ketamine causes hyperexcitability and involuntary muscle movements. When used in horses, pretreat with a sedative (e.g.,  $\alpha_2$  agonist).

### Drug Interactions

Ketamine hydrochloride is maintained at an acidic pH for stability and solubility. If mixed with alkalinizing solutions, instability or precipitation can result.

## Instructions for Use

Ketamine is often used in combination with other anesthetics and anesthetic adjuncts, such as xylazine, dexmedetomidine, medetomidine, acepromazine, opiates, propofol, lidocaine, and benzodiazepines (e.g., diazepam). Constant-rate infusions may be used to maintain a plane of anesthesia and analgesia. (See [dose](#) section for infusion doses.) Intravenous doses are generally less than intramuscular (IM) doses. In cats, ketamine may be sprayed into the mouth (10 mg/kg) and produces similar effects as IM injection. Animals receiving ketamine will have open eyelids, and artificial tears should be applied to prevent corneal injury.

## Patient Monitoring and Laboratory Tests

Monitor heart rate and breathing in patients anesthetized with ketamine. Although plasma concentrations are not typically monitored, the concentration of 0.22-0.37 mcg/mL is associated with analgesic properties in cats and 0.1-0.2 mcg/mL in people.

## Formulations

- Ketamine is available in 100-mg/mL injection solution.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ketamine is soluble in water and ethanol. Ketamine hydrochloride has been successfully administered when combined in a syringe immediately prior to injection with drugs such as  $\alpha_2$  agonists, propofol, guaifenesin, benzodiazepines, and acepromazine. Ketamine has been mixed with propofol at a ratio of 1:1 in the same syringe and administered intravenously.

## Small Animal Dosage

- For all animals: Lower doses listed for IV use; higher doses listed for IM use.

### Dogs

- 5.5-22 mg/kg IV or IM. (Generally, the lower dose range is given IV compared to IM.) It is recommended to use adjunctive sedative or tranquilizer treatment.
- CRI for perioperative use: Loading dose of 0.3-0.5 mg/kg IV, followed by 0.3-0.6 mg/kg/hr (5-10 mcg/kg/min), followed by 0.12 mg/kg/hr after surgery (18 hours). The rate during surgery may be increased to 1 mg/kg/hr if needed. To administer a rate of 0.3-0.6 mg/kg/hour, mix 0.6 mL (60 mg) with 1 L of fluids and infuse at a rate of 5-10 mL/kg per hour.
- CRI for light sedation: 1-2 mg/kg/hr, which may be combined with other sedatives.
- Combination of morphine/lidocaine/ketamine (MLK): Mixed as 100 mg/mL ketamine (1.6 mL/500 mL fluids) + 20 mg/mL lidocaine (30 mL/500 mL fluids), and 15 mg/mL morphine (1.6 mL/500 mL fluids) and infused at a rate of morphine: 0.24 mg/kg/hr; lidocaine: 3 mg/kg/hr; and ketamine: 0.6 mg/kg/hr, administered as CRI for perioperative analgesia.

### Cats

- 2-25 mg/kg IV or IM. (Generally, the lower dose range is given IV compared to IM.)  
**Note:** When used in cats, a sedative such as acepromazine (0.1 mg/kg) or a benzodiazepine is recommended prior to, or combined in same syringe with, administration of ketamine. When combined in same syringe, inject immediately after mixing. (In cats, it also can be sprayed into the mouth and produces similar effect as IM 10 mg/kg.)
- Short-term procedures: 3-5 mg/kg ketamine + 25 mcg/kg dexmedetomidine, mixed together, and administered IM (an opiate also may be included).
- Mix with propofol combined 1:1 in the same syringe at a dose of 2 mg/kg ketamine and 2 mg/kg propofol administered IV, followed by infusion (CRI) of 10 mg/kg/hr (both drugs combined).
- CRI: Loading dose of 0.3-0.5 mg/kg IV, followed by 0.3-0.6 mg/kg/hr (5-10 mcg/kg/min). This rate may be increased to 1 mg/kg/hr (15 mcg/kg/min) if needed, or lowered to 2-5 mg/kg/min when combined with other drugs (e.g., opiates).

## Large Animal Dosage

### Horses, Cattle, Sheep, and Swine

- 2 mg/kg IV (in horses, pretreat with a sedative).
- Ketamine at 1.1 mg/kg mixed with xylazine at 0.5 mg/kg may be combined in the same syringe and administered IV.
- CRI: Loading dose of 0.6 mg/kg IV, followed by CRI of 0.4-0.8 mg/kg/hr, and increased to 1.2 mg/kg/hr if needed. To prepare CRI solution for analgesia, add 30 mL ketamine to 1 liter bag of fluids (3 mg/mL), and administer IV over a duration of 8 hours at a rate of 125 mL per hour for average size horse.



- Equine “triple drip” consists of 500 mg xylazine plus 2,000 mg ketamine, added to 1 liter of 5% guaifenesin in dextrose. Infused at a rate of 1.1 mL/kg for induction, then 2.4 mL/kg per hour for maintenance.
- 10 mg/kg IM. Often used in combination with other agents, such as xylazine.
- Foals, treatment of seizures: 0.02 mg/kg/min CRI.

### Regulatory Information

Extralabel use: Withdrawal time of at least 3 days for meat and 48 hours for milk.

Schedule III controlled drug

Racing Commissioners International (RCI) classification: 2

## Ketoconazole

kee-toe-kah'nah-zole

**Trade and other names:** Nizoral

**Functional classification:** Antifungal

### Pharmacology and Mechanism of Action

Azole (imidazole) antifungal drug. Ketoconazole has a similar mechanism of action as other azole antifungal agents (itraconazole and fluconazole). It inhibits a P450 enzyme in fungi and inhibits ergosterol synthesis in the fungal cell membrane. Fungistatic. It has antifungal activity against dermatophytes and a variety of systemic fungi, such as *Histoplasma*, *Blastomyces*, and *Coccidioides* and *Malassezia* yeast. Other azole antifungal drugs include voriconazole, itraconazole, posaconazole, and fluconazole.

### Indications and Clinical Uses

Ketoconazole is used in dogs, cats, and some exotic animals to treat dermatophytes and systemic fungi, such as *Blastomyces*, *Histoplasma*, and *Coccidioides*. It also has been shown effective for treatment of *Malassezia* dermatitis. It does not have good activity against *Aspergillus*. Ketoconazole should not be used in horses because oral absorption is poor unless administered with a highly acidic vehicle. In dogs, it has a profound effect on cytochrome P450 enzymes and will inhibit metabolism of many drugs. This property has been used to reduce doses of cyclosporine (ketoconazole dose of 5-10 mg/kg). It is also via the inhibition of steroid P450 biosynthesis that ketoconazole has been used as a treatment for canine hyperadrenocorticism (canine Cushing disease).

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects in animals include dose-related vomiting (most common), diarrhea, hepatic injury, and rare thrombocytopenia in dogs. Liver enzyme elevations are common. Ketoconazole inhibits hormone synthesis and can lower concentrations of cortisol, testosterone, and other hormones in animals. Ketoconazole may produce a lighter hair coat color in some animals. It has been associated with cataract formation in dogs.

#### Contraindications and Precautions

Do not administer to pregnant animals. At high doses in laboratory animals, it caused embryotoxicity and fetal abnormalities. Some of these effects on pregnancy may be because of the inhibition of estrogen synthesis by ketoconazole.

### Drug Interactions

Ketoconazole is a potent inhibitor of hepatic and intestinal cytochrome P450 enzymes and P-glycoprotein and will inhibit metabolism of other drugs (anticonvulsants, cyclosporine, warfarin, and cisapride). Particular caution should be exercised when administering ketoconazole with ivermectin. This combination may produce ivermectin toxicity by decreasing clearance and enhancing penetration across the blood–brain barrier.

### Instructions for Use

Oral absorption depends on acidity in the stomach. Do not administer with antisecretory drugs or antacids. Because of endocrine effects, ketoconazole has been used for short-term treatment of hyperadrenocorticism. However, many experts believe that ketoconazole is not an effective long-term treatment for canine Cushing disease.

### Patient Monitoring and Laboratory Tests

Monitor liver enzymes (alanine aminotransferase [ALT], alkaline phosphatase [ALP]) for evidence of toxicity. Ketoconazole will lower serum cortisol levels.

### Formulations

- Ketoconazole is available in 200-mg tablets and 100-mg/mL oral suspension (Canada).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ketoconazole is practically insoluble in water but is soluble in ethanol. When ketoconazole was compounded extemporaneously from tablets with syrups and flavorings, it was stable for 60 days. However, ketoconazole requires acidity for solubility and may not be absorbed from these formulations. If compounded in alkaline conditions, it may precipitate.

### Small Animal Dosage

#### Dogs

- 10–15 mg/kg q8–12h PO.
- *Malassezia* infection: 5 mg/kg q24h PO every 3 weeks.
- Hyperadrenocorticism: Start with 5 mg/kg q12h initially, then increase after 7 days to 12–15 mg/kg q12h PO.

#### Cats

- 5–10 mg/kg q8–12h PO.

### Large Animal Dosage

#### Horses

Poorly absorbed. Fluconazole, itraconazole, or voriconazole is more completely absorbed.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Ketoprofen

kee-toe-proe'fen

**Trade and other names:** Orudis-KT (human over-the-counter [OTC] tablet), Ketofen (veterinary injection), and Anafen (outside the US.)

**Functional classification:** Nonsteroidal anti-inflammatory drug (NSAID)

## **Pharmacology and Mechanism of Action**

Ketoprofen, like other NSAIDs, produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the cyclo-oxygenase (COX) enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal physiologic functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Ketoprofen is a nonselective inhibitor of COX-1 and COX-2. There is weak evidence of its ability to inhibit lipooxygenase.

## **Indications and Clinical Uses**

Ketoprofen is an NSAID and is used for treatment of moderate pain and inflammation. It has a half-life in most animals of less than 2 hours, but it has a duration of action for up to 24 hours. Ketoprofen is not approved in the United States for small animals, but has been labeled for dogs and cats in other countries. It has been given by injection for acute treatment and by tablet for long-term use. In dogs and cats, it has been shown effective for treating pyrexia. In horses, ketoprofen is used for musculoskeletal inflammation and pain, abdominal pain, and other inflammatory conditions. Ketoprofen also has been used in cattle, goats, sheep, and pigs. In cattle, it has been effective for fever, pain, and inflammation associated with mastitis. It is approved for use in cattle in Canada but not in the US.

## **Precautionary Information**

### **Adverse Reactions and Side Effects**

All NSAIDs share the similar adverse effect of GI toxicity. The most common side effect is vomiting. Gastrointestinal ulceration is possible in some animals. Ketoprofen has been administered for 5 consecutive days in dogs without serious adverse effects, but longer treatment should be avoided. Dogs that received ketoprofen for 30 consecutive days (0.25 mg/kg per day) induced pyloric lesions and fecal occult blood. In horses, ketoprofen has been less ulcerogenic than phenylbutazone or flunixin meglumine in one study. Bleeding problems can occur if ketoprofen is administered before or after surgery.

### **Contraindications and Precautions**

Do not administer to animals prone to GI ulcers. Do not administer with other ulcerogenic drugs such as corticosteroids. Do not use extended-release formulations of ketoprofen.

### **Drug Interactions**

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

## **Instructions for Use**

Although not approved in the US, ketoprofen is approved for small animals in other countries. Doses listed are based on approved use in those countries. It is available as an OTC drug for humans in the US. In the US if it is used in small animals, either the large-animal injectable formulation or the human oral OTC tablets are used.

## **Patient Monitoring and Laboratory Tests**

Monitor patient for signs of GI intoxication (vomiting and diarrhea). Monitor renal function during chronic treatment.

## Formulations

- Ketoprofen is available in 12.5-mg tablets (OTC); 25, 50, and 75 mg (human preparation); and 100-mg/mL injection for horses. It is available in 10 mg/mL outside the US.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ketoprofen is insoluble in water, but it is soluble in ethanol. Stability of oral compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 1 mg/kg q24h PO for up to 5 days. Initial dose can be given via injection at up to 2 mg/kg SQ, IM, or IV.

## Large Animal Dosage

### Horses

- 2.2-3.3 mg/kg/day IV or IM.

### Pigs

- 3 mg/kg/day, PO, IV or IM.

### Cattle and Small Ruminants

- 3 mg/kg/day IV or IM for up to 3 days.

## Regulatory Information

Extralabel use in US: Withdrawal time of at least 7 days for meat and 24-48 hours for milk at a dose of 3.3 mg/kg q24h IM or IV. However, in other countries the withdrawal times are shorter. For example, it is approved in Canada.

For swine and cattle with a meat withdrawal time of 1 day.

RCI classification: 4

## Ketorolac Tromethamine

kee-toe'role-ak troe-meth'eh-meen

**Trade and other names:** Toradol

**Functional classification:** Nonsteroidal anti-inflammatory drug

## Pharmacology and Mechanism of Action

Ketorolac is a nonsteroidal anti-inflammatory drug (NSAID) that is a derivative of heteroaryl acetic acid. Ketorolac, like other NSAIDs, produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the COX enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal physiologic functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Ketorolac is a nonselective inhibitor of COX. There is some evidence that ketorolac also may affect opioid receptors centrally to produce analgesia, but it does not directly bind to opioid receptors. In some human studies it has had comparable efficacy to morphine. The pharmacokinetics have been studied in dogs, but not other species.

## 434 Ketorolac Tromethamine

In dogs it has a half-life of approximately 4.5 or 10 hours (depending on the study) and a variable volume of distribution of 0.3 - > 1 L/kg, depending on the study with protein binding of 99%.

### Indications and Clinical Uses

Ketorolac is infrequently used in veterinary medicine. There are only limited data on safety and efficacy for veterinary uses. It has occasionally been used to treat pain and inflammation in dogs. The most common use has been for treatment of pain associated with surgery in dogs.

### Precautionary Information

#### Adverse Reactions and Side Effects

Like other NSAIDs, it may cause GI ulceration and renal ischemia. Ketorolac may cause GI lesions if administered more frequently than every 8 hours.

#### Contraindications and Precautions

Do not administer more than two doses. Do not administer to animals prone to GI ulcers. Do not administer with other ulcerogenic drugs such as corticosteroids.

#### Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and ACE inhibitors.

### Instructions for Use

Limited clinical studies in dogs have been conducted. However, it may be effective in some patients for short-term use. Long-term administration is discouraged.

### Patient Monitoring and Laboratory Tests

Monitor for signs of GI ulceration. Plasma concentrations are not generally monitored but levels of 0.1-0.3 mcg/mL in people are considered in the analgesic range.

### Formulations

- Ketorolac is available in 10-mg tablets and 15- and 30-mg/mL injection in 10% alcohol.

### Stability and Storage

Store in a tightly sealed container, protected from light and humidity, and at room temperature. Ketorolac tromethamine is soluble in water and slightly soluble in ethanol. Stability of oral compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 0.5 mg/kg q8-12h PO, IM, or IV.

#### Cats

- No safe dose is established.

### Large Animal Dosage

- No large animal doses are reported.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Lactated Ringer's Solution

**Trade and other names:** LRS

**Functional classification:** Fluid replacement

### Pharmacology and Mechanism of Action

Lactated Ringer's solution is a fluid solution for replacement intended for intravenous (IV) administration. Lactated Ringer's solution contains a balanced combination of electrolytes and an alkalinizing buffer. This solution contains 28 mEq/L of lactate.

### Indications and Clinical Uses

Lactated Ringer's solution is indicated as a replacement or maintenance fluid. It also is used as a vehicle to deliver IV medications via constant-rate infusion (CRI). It has been administered subcutaneously, intraosseously (in bone medullary cavity), and intraperitoneally (IP) in animals when IV access is not possible. It contains lactate, a metabolizable base, but will not correct acidosis as quickly as bicarbonate. Severely acidemic animals may already have high lactate serum levels.

### Precautionary Information

#### Adverse Reactions and Side Effects

No significant adverse effects.

#### Contraindications and Precautions

Administer IV fluids only in patients monitored carefully.

#### Drug Interactions

Lactated Ringer's solution has a pH of 6-7.5. Do not add medications to this solution if they are unstable at this pH. Lactated Ringer's contains calcium. Do not add drugs to this solution that may bind (chelate) to calcium.

### Instructions for Use

Fluid requirements vary depending on animal's needs (replacement vs. maintenance). For shock therapy, administer one half the calculated dose in the first 30 minutes and in 10-mL/kg increments every 15 minutes, followed by a CRI. For severe acidemia, consider fluids supplemented with bicarbonate instead of lactate. Fluid rates used in dogs and cats during anesthesia have previously been 10 mL/kg/hr, IV, but these recommendations have been lowered to 3 mL/kg/hr in cats and 5 mL/kg/hr in dogs. See dosing section for calculation of maintenance rates.

### Patient Monitoring and Laboratory Tests

Monitor patient's hydration status and electrolyte balance (especially potassium, chloride, and sodium). With high administration rates, monitor patient for signs of pulmonary edema.

### Formulations

- Lactated Ringer's solution is available in 250-, 500-, and 1000-mL fluid bags.

### Stability and Storage

Store in a tightly sealed container. If container has been punctured or transferred to another container, sterility cannot be assured.

## Small Animal Dosage

### Dogs and Cats

- Moderate dehydration: 15-30 mL/kg/hr IV.
- Severe dehydration: 50 mL/kg/hr IV.
- Maintenance rates:
  - Cat: 2-3 mL/kg/hr.
  - Dog: 2-6 mL/kg/hr.
- Maintenance (per day): 55-65 mL/kg/day IV, SQ, or IP (2.5 mL/kg/hr).
- During anesthesia: Initial rate 3 mL/kg/hr for cats and 5 mL/kg/hr for dogs IV. If necessary to replace losses, increase to 10 mL/kg/hr IV.
- Shock therapy: 90 mL/kg IV (for dogs) and 60-70 mL/kg IV (for cats).

## Large Animal Dosage

### Cattle, Horses, and Pigs

- Maintenance: 40-50 mL/kg/day IV.
- Moderate dehydration: 15-30 mL/kg/hr IV.
- Severe dehydration: 50 mL/kg/hr IV.

### Calves and Foals

- Moderate dehydration: 45 mL/kg at a rate of 30-40 mL/kg/hr IV.
- Severe dehydration: 80-90 mL/kg at a rate of 30-40 mL/kg/hr IV. In severe cases, it may be given as rapidly as 80 mL/kg/hr.

## Regulatory Information

There is no risk of harmful residues in animals intended for food. No withdrawal times are necessary.

## Lactulose

lak'tyoo-lose

**Trade and other names:** Chronulac and generic brands

**Functional classification:** Laxative

## Pharmacology and Mechanism of Action

Laxative. Lactulose is a disaccharide sugar containing one molecule of fructose and one molecule of galactose. Lactulose produces a laxative effect by osmotic effect in the colon. It is a nonabsorbed sugar and retains water in the intestine after oral administration via an osmotic effect. Lactulose also will decrease the pH of the intestinal lumen.

## Indications and Clinical Uses

Lactulose is administered orally for treatment of hyperammonemia (hepatic encephalopathy) because it decreases blood ammonia concentrations via lowering the pH of the colon; thus ammonia in the colon is not as readily absorbed. Lactulose also is administered orally to produce a laxative effect for treatment of constipation.

## Precautionary Information

### Adverse Reactions and Side Effects

Excessive use may cause fluid and electrolyte loss.

**Contraindications and Precautions**

Use lactulose with caution in animals with diabetes because it contains lactose and galactose.

**Drug Interactions**

No drug interactions are reported for animals.

**Instructions for Use**

In veterinary medicine, clinical studies to establish efficacy are not available. In addition to doses cited, 20-30 mL/kg of 30% solution retention enema has been used in cats.

**Patient Monitoring and Laboratory Tests**

When used for treating hepatic encephalopathy, monitor the patient's hepatic status.

**Formulations**

- Lactulose is available in 10-g/15 mL liquid solution (3.3 g per 5 mL).

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water. Darkening of the solution may occur without affecting stability. Avoid freezing.

**Small Animal Dosage****Dogs**

- Constipation: 1 mL/4.5 kg q8h (to effect) PO.
- Hepatic encephalopathy: 0.5 mL/kg q8h PO.

**Cats**

- Constipation: 1 mL/4.5 kg q8h (to effect) PO.
- Hepatic encephalopathy: 2.5-5 mL/cat q8h PO.

**Large Animal Dosage****Horses and Cattle**

- 0.25-0.5 mL/kg/day PO.

**Regulatory Information**

There is little risk of residues in animals intended for food. No withdrawal times are necessary.

**Leflunomide**

le-FLOO-noe-mide, or leh-FLEW-nah-mide

**Trade and other names:** Arava and generic

**Functional classification:** Immunosuppressive drug

**Pharmacology and Mechanism of Action**

Leflunomide is an isoxazole immunosuppressive drug. Leflunomide is not active as the parent drug, but it is converted to an active metabolite A77 1726 (also known as M1 and teriflunomide), which inhibits T-cell and B-cell proliferation and is responsible for clinical immunosuppressive effects. It inhibits the synthesis of pyrimidine via



inhibition of the enzyme dihydroorotate dehydrogenase. This enzyme is important for the de novo pyrimidine synthesis, which is critical for function of activated and stimulated lymphocytes. It also may produce anti-inflammatory effects by inhibiting proinflammatory cytokines.

After oral absorption, the plasma levels of leflunomide are low or undetectable. Therapeutic effects are produced from the metabolite A77 1726 (M1) for the immunosuppressive action. If monitoring is performed, the measurement should focus on the metabolite concentrations. In people, the metabolite M1 has a very long half-life of approximately 2 weeks. But in studies performed in experimental dogs, the half-life was only 21-25 hours, and the peak concentrations were much lower than in people. In people, the long half-life requires several days to accumulate to steady-state levels and to decline from a peak level. Loading doses are often administered in people. However, because of the shorter half-life, loading doses are not needed in dogs, and steady-state concentrations will be attained in approximately 5 days. In cats, the half-life is 60 hours with complete oral absorption.

### **Indications and Clinical Uses**

This drug is used in people primarily for rheumatoid arthritis. In dogs, it has been used for a variety of immune-mediated diseases as a substitute for other drugs such as azathioprine or mycophenolate. These diseases include myasthenia gravis, Evan syndrome, immune-mediated hemolytic anemia and thrombocytopenia, and polymyositis/polyarthritis. Efficacy has not been studied in controlled clinical studies, but in reported anecdotal observations or from uncontrolled retrospective studies. In one case report, there was a positive response in most dogs with immune-mediated polyarthritis treated at 3-4 mg/kg once daily.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

The most common adverse effects in dogs have been decreased appetite and diarrhea. Adverse gastrointestinal (GI) effects are more common with higher doses. Because of the GI effects, many clinicians start with a low dose and gradually titrate up to higher doses. Mild anemia and lethargy also have been observed. Although rare, leukopenia is possible with doses >4 mg/kg, and periodic complete blood count (CBC) to monitor patients is recommended. In cats, the most common adverse effects have been intermittent vomiting, which is mild and transient.

#### **Contraindications and Precautions**

Do not administer to pregnant animals. This drug can be toxic to a developing fetus.

#### **Drug Interactions**

No interactions are reported.

### **Instructions for Use**

Leflunomide is used most often in dogs for immunosuppressive treatment when other drugs have failed or when the patient has become refractory to other drugs and a substitute is considered. The dosing protocols used currently are derived from extrapolation and some anecdotal reports. Most veterinarians start with 4 mg/kg per day, then lower the dose as the patient responds. Pharmacokinetic studies in dogs suggest that the dose of 4 mg/kg per day may not produce drug levels that are considered therapeutic. Therefore in patients that have not responded, there should be consideration for higher doses.

### Patient Monitoring and Laboratory Tests

Monitor CBC and platelet counts in treated animals. Anemia has been reported as a consequence of treatment. If blood monitoring is pursued, plasma samples may be collected and measured for A77 1726 (the active metabolite). This metabolite is stable in serum for up to 5 months under refrigerated conditions. Drug concentrations at 12 hours (trough) are considered effective if greater than 20 mcg/mL.

### Formulations

- Available in 5-, 10-, and 20-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 4 mg/kg per day, usually in divided doses of 2 mg/kg q12h, tapered to 2 mg/kg q24h PO. After an induction period, the dose may be decreased by 25% increments until the patient is stabilized or until the disease resolves. Some patients may require higher starting doses.

#### Cats

- 2 mg/kg per day, for 2 days, PO, then 2 mg/kg q48h PO.

### Large Animal Dosage

- No large animal doses are available.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

## Leucovorin Calcium

loo-koe-vor'in kal'see-um

**Trade and other names:** Wellcovorin and generic brands

**Functional classification:** Antidote

### Pharmacology and Mechanism of Action

Leucovorin is a reduced form of folic acid that is converted to active folic acid derivatives for purine and thymidine synthesis.

### Indications and Clinical Uses

Use of leucovorin is uncommon in animals. It may be used as an antidote for folic acid antagonists. In humans, it is primarily used as rescue for overdoses of folic acid antagonists (methotrexate) and treatment of adverse reactions from methotrexate, but also may be considered for reactions caused by pyrimethamine and trimethoprim.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse reactions reported for animals, but allergic reactions have been reported in people.

**Contraindications and Precautions**

No contraindications reported for animals.

**Drug Interactions**

Leucovorin will interfere with the action of trimethoprim and pyrimethamine.

**Instructions for Use**

Clinical studies have not been reported in veterinary medicine. Although leucovorin may prevent toxicity from trimethoprim, it will not prevent toxic reactions that may be caused by sulfonamides in animals.

**Patient Monitoring and Laboratory Tests**

Monitor CBC if this drug is used to treat overdose of folic acid antagonists.

**Formulations Available**

- Leucovorin is available in 5-, 10-, 15-, and 25-mg tablets and 3- and 5-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water but is insoluble in ethanol. Reconstituted solutions have stability for 7 days at room temperature or refrigerated.

**Small Animal Dosage****Dogs and Cats**

- With methotrexate administration: 3 mg/m<sup>2</sup> IV, IM, or PO.
- As antidote for pyrimethamine toxicosis: 1 mg/kg q24h PO.

**Large Animal Dosage**

- No large animal doses are reported. However, if pyrimethamine toxicosis is suspected in horses, doses listed for small animals may be considered.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use with withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Levamisole Hydrochloride**

leh-vam'ih-sole hye-droe-klor'ide

**Trade and other names:** Levasole, Ripercol, Tramisol, and Ergamisol

**Functional classification:** Antiparasitic

**Pharmacology and Mechanism of Action**

Levamisole is an antiparasitic drug of the imidazothiazole class. It eliminates a variety of parasites via neuromuscular toxicity. Levamisole has an immunorestorative effect in animals, but the mechanism of action on the immune system is unknown. It may activate and stimulate proliferation of T-cells; augment monocyte activation; and stimulate macrophages, including phagocytosis and chemotaxis. It may increase neutrophil mobility. However, it is not cytotoxic to neutrophils or immune cells.

## Indications and Clinical Uses

In cattle and sheep, it is used to treat a variety of nematodes, including stomach worms (*Haemonchus*, *Trichostrongylus*, and *Ostertagia* spp.), intestinal worms (*Trichostrongylus*, *Cooperia*, *Nematodirus*, *Bunostomum*, *Oesophagostomum*, and *Chabertia* spp.), and lungworms (*Dictyocaulus* spp.). In pigs, it is used to treat nematodes such as large roundworms (*Ascaris suum*), nodular worms (*Oesophagostomum* spp.), intestinal thread worms (*Strongyloides ransomi*), and lungworms (*Metastrongylus* spp.). Levamisole has been used for treatment of endoparasites in dogs and as a microfilaricide. Macrocytic lactones (e.g., milbemycin oxime or ivermectin) are considered a preferred heartworm microfilaricide. In people, levamisole is used as an immunostimulant to aid in treatment of colorectal carcinoma and malignant melanoma. In animals, levamisole also is used as an immunostimulant, but reports of efficacy are lacking.

## Precautionary Information

### Adverse Reactions and Side Effects

Levamisole may produce cholinergic toxicity. It has produced vomiting in some dogs. The injectable formulation has caused some swelling at the site of injection. In humans, when used as an immunostimulant, it has caused stomatitis, agranulocytosis, and thrombocytopenia.

### Contraindications and Precautions

Use cautiously in animals with high heartworm microfilaria burdens. Reactions are possible from heavy kill rate of microfilaria. There are no adverse reactions on fertility and no effects on pregnancy. In rats and rabbits, there was no evidence of teratogenicity or embryotoxicity at doses of 180 mg/kg. Levamisole is abused in people and often mixed with cocaine to either potentiate the effects to produce additional central nervous system (CNS) stimulation, or is added as a marker compound. When used in this form in people, it has produced agranulocytosis in some individuals. Levamisole may potentially be converted to aminorex, a CNS stimulant in horses with amphetamine properties, which may affect performance.

### Drug Interactions

Do not use with pyrantel because they share the same mechanism of toxicity.

## Instructions for Use

In heartworm-positive dogs, it may sterilize female adult heartworms. Levamisole has also been used as an immunostimulant; however, clinical reports of its efficacy are not available. Because of the possibility of contamination at the injection site, use a clean needle with each animal and clean the injection site.

## Patient Monitoring and Laboratory Tests

Monitor for microfilaria before treatment because of risk of reaction with a high heartworm burden.

## Formulations

- Levamisole is available in 0.184-g bolus; 2.19-g bolus; 9-, 11.7-, and 18.15-g per packet; 136.5-mg/mL and 182-mg/mL injection (levamisole phosphate); and 50-mg tablet. Also available in U.S. as 46.8 gram packet for cattle and sheep, and 18.15 gram bottle for pigs.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- Endoparasites: 5-8 mg/kg once PO (up to 10 mg/kg PO for 2 days).
- Hookworms: 10 mg/kg/day for 2 days.
- Microfilaricide: 10 mg/kg q24h PO for 6-10 days (recommended to use macrocyclic lactones instead).
- Immunostimulant: 0.5-2 mg/kg 3 times/week PO. (In humans, the immunostimulant dose is given q8h for 3 days.)

### Cats

- Endoparasites: 4.4 mg/kg once PO.
- Lungworms: 20-40 mg/kg q48h for 5 treatments PO.

## Large Animal Dosage

### Cattle and Sheep

- 8 mg/kg once PO, or approximately one 2.19-g bolus per 450-750 pounds (200-340 kg).
- Levamisole injection (for cattle): 8 mg/kg SQ into midneck area once, or approximately 2 mL per 100 pounds (45 kg).

### Pigs

- 8 mg/kg in drinking water.

## Regulatory Information

Cattle withdrawal time for meat: 2 days (PO) and 7 days (SQ injection).

Sheep withdrawal time for meat: 3 days.

Pig withdrawal time (meat): 3 days.

Horses: There are some reports that levamisole can be converted to aminorex in horses, which is a CNS stimulant and a banned substance in racing horses.

## Levetiracetam

lev-eh-teer-ass'eh-tam

**Trade and other names:** Keppra

**Functional classification:** Anticonvulsant

## Pharmacology and Mechanism of Action

Anticonvulsant. The mechanism of action is not certain, but it does not involve inhibitory neurotransmitters. It inhibits burst firing of neurons without affecting normal neuronal excitement. It does not undergo hepatic metabolism, but may undergo metabolism that does not include cytochrome P450 enzymes. Elimination relies on renal clearance.

## Indications and Clinical Uses

In dogs, levetiracetam has been used to treat seizures, especially those refractory to other anticonvulsants. In dogs, it has been considered a drug of choice as an add-on medication when patients are refractory to phenobarbital and bromide therapy. It often is used in combination with other anticonvulsants. Clinical efficacy as an add-on medication with phenobarbital and bromide is uncertain. In dogs, the oral absorption is 100%, the half-life is 3-4 hours, and the volume of distribution is 0.4-0.5 L/kg. Levetiracetam has been used to treat seizure disorders in cats at a dose of 20 mg/kg

every 8 hours and found to be effective in some cases. In cats, the oral absorption is also 100%, with a half-life of 3 hours and a volume of distribution similar to dogs.

### Precautionary Information

#### Adverse Reactions and Side Effects

Weakness, lethargy, and dizziness have been reported in people. Adverse effects have been rare in animals, except for occasional lethargy and decreased appetite. Oral administration can produce hypersalivation in cats.

#### Contraindications and Precautions

No known contraindications.

#### Drug Interactions

Ordinarily, there are no direct interactions with drugs that inhibit or induce cytochrome P450 enzymes. However, studies in dogs and people have confirmed that phenobarbital can enhance the clearance of levetiracetam. For example, the half-life is shorter and clearance is more rapid when dogs are administered phenobarbital simultaneously. The mechanism for the interaction is unknown, but may warrant higher doses, or more careful monitoring when levetiracetam is used with phenobarbital. Interactions with other concurrently used anticonvulsants have not been reported.

### Instructions for Use

It is rapidly and completely absorbed, and absorption is not affected by feeding. An injectable formulation is available but not used often in veterinary medicine. However, the injectable solution has been administered at a dose of 20 mg/kg IV bolus increments to a maximum of 60 mg/kg in emergency situations. Levetiracetam ordinarily should be administered every 8 hours to maintain effective concentrations. Higher doses may be needed if administered with phenobarbital because phenobarbital significantly increases clearance in dogs. The extended-release (XR) tablets may have longer effects and can be administered every 12 hours to dogs.

### Patient Monitoring and Laboratory Tests

Monitor seizure frequency. Currently no clinical monitoring test for serum exists in routine laboratories. However, some laboratories have this capability. Therapeutic plasma/serum concentrations in people are in the range of 10-40 mcg/mL.

### Formulations

- Levetiracetam is available in 250-, 500-, 750-, and 1000-mg tablets. Extended-release formulation (XR) available in 500-, 750-, and 1000 mg-tablets. Oral solution 100 mg/mL, and 100- and 500-mg/mL solution for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. It is soluble in water, and it may be acceptable to mix with other foods, syrups, or flavorings immediately prior to oral administration.

### Small Animal Dosage

#### Dogs

- 20 mg/kg q8h PO. More frequent administration or higher doses may be necessary with concurrent phenobarbital treatment.
- Oral extended-release tablets: 30 mg/kg q12h PO.
- Intravenous use (emergency situations): 20 mg/kg IV bolus, repeated if necessary, up to 60 mg/kg. Duration of injection is approximately 3 hours.

## 444 Levodopa

- Rectal administration: 40 mg/kg rectal administration (100 mg/mL solution) has produced effective concentrations in experimental dogs. However, in most dogs, the volume is too large to be practical.

### Cats

- 20-mg/kg q8h PO.

## Large Animal Dosage

### Horses

- 30 mg/kg IV for short-term treatment, or 30 mg/kg q24h PO.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Levodopa

lee'voe-doe'pah

**Trade and other names:** Larodopa and L-dopa

**Functional classification:** Dopamine agonist

## Pharmacology and Mechanism of Action

Dopamine, when administered systemically, does not cross the blood–brain barrier. However, levodopa crosses more easily via a carrier-mediated process and is converted to dopamine after crossing the blood–brain barrier. Dopamine is used in neurodegenerative disorders to stimulate CNS dopamine receptors.

## Indications and Clinical Uses

In people, levodopa is used for treating Parkinson disease, and it is used in combination with carbidopa (a peripheral decarboxylase inhibitor) and entacapone (an o-methyltransferase inhibitor) to potentiate therapy. In animals, it has been used for treating hepatic encephalopathy.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects in animals have not been reported. In people, dizziness, mental changes, difficult urination, and hypotension are among the reported adverse effects.

### Contraindications and Precautions

There are no specific contraindications for use in animals.

### Drug Interactions

Antidopamine drugs will interfere with action. Such drugs include metoclopramide, phenothiazines (e.g., acepromazine), and risperidone.

## Instructions for Use

Clinical studies have not been reported in veterinary medicine. The use, and doses, have been extrapolated from human use. Titrate dose for each patient.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Levodopa is available in 100-, 250-, and 500-mg tablets or capsules.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Levodopa is slightly soluble in water but more soluble in acid solutions. It will be rapidly oxidized with exposure to air, which will be indicated by a darkening of the formulation. Injectable solutions have been prepared extemporaneously and found to be stable for 96 hours.

## Small Animal Dosage

### Dogs and Cats

- Hepatic encephalopathy: 6.8 mg/kg initially PO, then 1.4 mg/kg q6h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available for animals intended for food. Because of low risk of residues, no withdrawal times are suggested.

## Levothyroxine Sodium

lee-voe-thye-roks'een soe'dee-um

**Trade and other names:** T<sub>4</sub>, L-thyroxine, Soloxine, Levocrine, Thyro-Tabs, Synthroid, ThyroMed. Leventa and equine powders include Equisyn-T<sub>4</sub>, Levo-Powder, Thyroid Powder, and Thyro-L.

**Functional classification:** Hormone

## Pharmacology and Mechanism of Action

Thyroid hormone. Levothyroxine is used as replacement therapy for treating patients with hypothyroidism. Levothyroxine is T<sub>4</sub>, which is converted in most patients to the active T<sub>3</sub>. Requirements and pharmacokinetics vary among animals, and doses are adjusted on the basis of thyroid monitoring. Levothyroxine has a half-life of approximately 20 hours in dogs. The oral solution has a half-life of approximately 12 hours, with a peak occurring at 5 hours.

## Indications and Clinical Uses

Levothyroxine is used for replacement therapy in animals with thyroid hormone deficiency (hypothyroidism). It has been used in many species, including dogs, cats, and horses. Although it has been suggested for use in treating dogs with von Willebrand disease, clinical studies failed to show an effect on clotting factors, bleeding times, or von Willebrand factor (vWf) from levothyroxine treatment (0.04 mg/kg).

Intravenous levothyroxine sodium may be used in dogs for acute treatment of hypothyroid dogs with myxedema coma (4-5 mcg/kg IV).

## Precautionary Information

### Adverse Reactions and Side Effects

High doses may produce thyrotoxicosis, but this is uncommon. Potential adverse effects from IV treatment include arrhythmias or pneumonia.



**Contraindications and Precautions**

No specific contraindications are reported for small animals. When switching from one brand to another, it is advised to follow up by testing to ensure that brands are therapeutically equivalent.

**Drug Interactions**

Patients receiving corticosteroids may have decreased ability to convert  $T_4$  to the active  $T_3$ . The following drugs may lower thyroid concentrations when administered to otherwise healthy animals: nonsteroidal anti-inflammatory drugs (NSAIDs), sulfonamides, and phenobarbital, although results in some dogs may not be clinically significant. Although not reported in animals, in people, administration of estrogens increases thyroid-binding globulin and may decrease the active form of thyroid hormone ( $T_4$ ) in patients receiving thyroid supplementation. Monitor  $T_4$  levels in these patients and increase dose of thyroxine if necessary. Feeding may decrease oral absorption.

**Instructions for Use**

Thyroid supplementation should be guided by testing to confirm diagnosis and post-medication monitoring to adjust dose. The brands Soloxine and Synthroid have been equivalent according to studies in dogs, but the oral liquid (Leventa) is absorbed 150%-200% more than the oral tablets, and dose adjustments should be considered when switching from oral tablets to oral liquid. For tablets, bioavailability is only 37% (average). When using the liquid formulation (Leventa), use the specially designed syringes for dosing. The starting dose listed in the dosing section for tablets in dogs (22 mcg/kg q12) may not be high enough for some dogs, and monitoring is recommended to adjust dose appropriately. When prescribing human formulations, it is a good idea to advise pharmacists that canine doses are much higher than human doses.

**Patient Monitoring and Laboratory Tests**

Monitor serum  $T_4$  concentrations to guide therapy. Normal thyroxine ( $T_4$ ) baseline levels are 20-55 nmol/L (1.5-4.3 mcg/dL). Thyrotropin-releasing hormone (TRH) injection should result in at least a 1.5-fold increase in  $T_4$ . To monitor postpill adequacy of therapy, some feel that the most valuable sample to collect is immediately prior to the next scheduled dose (trough level). Alternatively, some clinicians take a peak concentration by collecting a blood sample 4-6 hours after administering the pill, and the  $T_4$  should be between 30 and 60 nmol/L (2.3 and 4.6 mcg/dL). If administering the oral liquid, the peak concentration occurs at 2-2.5 hours. In horses, postpill peak occurs at 1-2 hours.

**Formulations**

- Levothyroxine is available in a range of sizes from 0.025- to 0.8-mg tablets (in 0.1-mg increments), 0.1- to 0.8-mg chewable tablets, 1.0-mg/mL oral solution for dogs, and 1-gram of thyroxine per 453.6 of oral powder (1 gram per pound of the oral powder) used for horses. Note that levothyroxine products for animals are not FDA-approved; therefore, it is not possible to establish bioequivalence of various products. Do not assume that all levothyroxine products are bioequivalent and produce the same response. When switching from one brand to another, follow-up testing is recommended to ensure the same response.

**Stability and Storage**

Levothyroxine is inherently unstable and can be markedly affected by heat, light, and humidity. Store in a tightly sealed container, protected from light, and at room temperature. Thyroxine is only slightly soluble in water or ethanol. It is more soluble at

pH <2 or >8. It has been unstable in some compounded formulations. However, it may be added to food products if administered immediately. Powder may be mixed with water and added to horse's grain every day. When it was mixed with ethanol followed by mixing with a syrup, it was stable for 15 days at room temperature and 47 days refrigerated. However, other compounded preparations have been stable for only 15 days (refrigerated) or 11 days (room temperature). Therefore use of compounded formulations should probably be limited to a storage time of 10-15 days.

The oral solution (Leventa) has an 18-month shelf-life when stored refrigerated, but once opened, it can be stored for 2 months at room temperature, protected from light, and for 6 months refrigerated.

## Small Animal Dosage

### Dogs

- 18-22 mcg/kg (0.018-0.022 mg/kg) q12h PO (adjust dose via monitoring); an alternative dose is 0.5 mg per square meter (0.5 mg/m<sup>2</sup>).
- Liquid (1 mg/mL): 20 mcg/kg PO q24h, but doses may range from 12-42 mcg/kg q24h after adjusting.
- IV therapy for acute treatment: 4-5 mcg/kg IV, administer once or as needed every 12 hr.

### Cats

- 10-20 mcg/kg/day (0.01-0.02 mg/kg) PO (adjust dose via monitoring).

## Large Animal Dosage

### Horses

- 10-60 mcg/kg (0.01-0.06 mg/kg) q24h or 5-30 mcg/kg (0.005-0.03 mg/kg) q12h PO. When using the oral powder for dosing in horses, 1 level teaspoon contains 12 mg of levothyroxine (T<sub>4</sub>), and 1 tablespoon contains 36 mg of levothyroxine (T<sub>4</sub>). This powder may be mixed in with daily ration of grain (e.g., 4 level teaspoons mixed with 30 mL water and added to oats per day).
- Horses with pituitary pars intermedia dysfunction (PPID): 0.1 mg/kg (48 mg per horse) per day.

## Regulatory Information

No regulatory information is available for animals intended for food. Because of low risk of residues, no withdrawal times are suggested.

## Lidocaine Hydrochloride

lye'doe-kane hye-droe-klor'ide

**Trade and other names:** Xylocaine and generic brands

**Functional classification:** Local anesthetic, antiarrhythmic

## Pharmacology and Mechanism of Action

Local anesthetic. Lidocaine inhibits nerve conduction via sodium channel blockade. Class-1 antiarrhythmic. Decreases Phase 0 depolarization without affecting conduction. After systemic administration, lidocaine is metabolized to monoethylglycinexylidide (MEGX), which also has antiarrhythmic properties. Lidocaine also has analgesic properties after systemic administration. During IV infusion, it may decrease pain response. In horses, infusions of lidocaine have decreased postoperative ileus either through a direct effect, via suppression of painful stimuli, or through anti-inflammatory effects on neutrophils. In dogs with GI compromise caused by gastric dilatation volvulus (GDV), it improved recovery by reducing the severity of ischemic reperfusion injury and inflammatory response.

Pharmacokinetics in dogs and cats are similar; however, cats have increased sensitivity to the cardiac effects. In horses, half-life ranges from 40 min to 80 min, with a high, but variable, clearance rate. In dogs the half-life is approximately 1 hour with a high clearance rate (30-40 mL/kg/min). In cats the pharmacokinetics are different than dogs with a longer half-life and slower clearance, making cats more susceptible to adverse effects than dogs. In cattle the half-life is approximately 1 hour.

### **Indications and Clinical Uses**

Lidocaine is used commonly as a local anesthetic and for acute treatment of ventricular arrhythmias. Lidocaine should be used cautiously for treating supraventricular arrhythmias because it may increase cardiac conduction. Lidocaine also is used for pain management. It has been administered as a CRI in animals, especially in postsurgical patients to improve recovery after intestinal or gastric surgery (see mechanism section). Lidocaine has been combined with other analgesics, which may be synergistic and allow lower doses of each individual component. One example of a combination is MLK, which is morphine (or fentanyl), lidocaine, and ketamine (see dosing section for formula). Lidocaine has been used on a limited basis to treat seizures that are refractory to other drugs. In horses, studies have confirmed that a lidocaine CRI may help to restore intestinal motility, and is used to treat intestinal ileus.

Lidocaine has been applied to animals as a transdermal patch. The patch (designed for people) is 5% strength and used primarily for neuropathic pain (postherpetic neuralgia). This patch also has been applied for some conditions in dogs and cats with anecdotal accounts of some success. Absorption from the patch is low (less than 5%), which is far below the threshold for toxic effects.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

High doses cause CNS effects (tremors, twitches, and seizures) and vomiting, but risk of lidocaine-induced seizures is low. Lidocaine can produce cardiac arrhythmias, but it has greater effect on abnormal cardiac tissue than normal tissue. Intravenous doses of lidocaine in cats have resulted in death. In cats under anesthesia, lidocaine administration has caused decreased cardiac output, cardiovascular depression, and decreased oxygen delivery to tissues. In cats, lidocaine has also produced methemoglobinemia and hemolysis. Intravenous use and CRIs in horses have caused muscle fasciculations, rapid eye blinking, anxiety, ataxia, weakness, and seizures.

#### **Contraindications and Precautions**

Cats are more susceptible to adverse effects, and lower doses should be used. Absorption from lidocaine patches in cats is only 6.3% and not expected to present a problem. In animals with decreased blood flow to liver (e.g., animals under anesthesia), clearance may be reduced. Constant-rate infusion in cats is lower than the rate in dogs.

#### **Drug Interactions**

Lidocaine hydrochloride is maintained as an acidic solution for solubility. Although short-term mixing with alkaline solutions may not interfere with stability (i.e., immediately prior to administration), storage in alkalinizing solutions can cause precipitation. If mixed with alkalinizing solutions, it should be administered promptly.

### **Instructions for Use**

When used for local infiltration, many formulations contain epinephrine to prolong activity at the injection site. Avoid using formulations that contain epinephrine in patients with cardiac arrhythmias. Note that human formulations may contain epinephrine, but no veterinary formulations contain epinephrine. To increase pH, speed onset of action,

and decrease pain from injection, one may add 1 mEq sodium bicarbonate to 10 mL lidocaine (use immediately after mixing). To prepare solutions for infusion in horses, mix 10 g of 2% lidocaine in 3 L of lactated Ringer's solution (0.33% solution).

### Patient Monitoring and Laboratory Tests

Monitor for signs of neurotoxicity (e.g., depression, muscle twitching, and seizures). Monitor electrocardiogram (ECG) during treatment for cardiac rate and rhythm in treated animals.

### Formulations

- Lidocaine is available in 5-, 10-, 15-, and 20-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Topical preparations have been prepared and found to be stable for several weeks.

### Small Animal Dosage

#### Dogs

- Antiarrhythmic: 2-4 mg/kg IV (to a maximum dose of 8 mg/kg over 10-minute period).
- Antiarrhythmic: 25-75 mcg/kg/min IV CRI.
- Antiarrhythmic: 6 mg/kg q1.5h IM.
- Epidural: 4.4 mg/kg of 2% solution.
- Adjunct to control pain and inflammation associated with surgery: 2 mg/kg IV bolus, followed by 0.05 mg/kg/minute CRI for 24 hours (added to patient's fluids).
- Combination of morphine/lidocaine/ketamine (MLK): mixed as 100 mg/mL ketamine (1.6 mL per 500 mL fluids), 20 mg/mL lidocaine (30 mL per 500 mL fluids), and 15 mg/mL morphine (1.6 mL per 500 mL fluids) and infused at a rate of morphine: 0.24 mg/kg hr, lidocaine: 3 mg/kg/hr, and ketamine: 0.6 mg/kg/hr, administered as CRI for perioperative analgesia.

#### Cats

- Antiarrhythmic: Start with 0.1-0.4 mg/kg initially and then increase to 0.25-0.75 mg/kg IV slowly if there has been no response.
- Antiarrhythmic: Loading dose of 0.5-1 mg/kg IV, followed by 10-20 mcg/kg/min (0.6-1.2 mg/kg/hr) IV CRI.
- Epidural: 4.4 mg/kg of 2% solution.

### Large Animal Dosage

#### Horses

- Antiarrhythmic: 0.25-0.5 mg/kg q5-15 min IV, for a total of 1.5 mg/kg, then as a CRI of 0.05 mg/kg/min (50 mcg/kg/min).
- Postoperative ileus: 1.3 mg/kg IV bolus administered over 15 min, followed by 0.05 mg/kg/min (50 mcg/kg/min) CRI.
- Analgesia: 2 mg/kg IV, followed by 50 mcg/kg/min CRI.

### Regulatory Information

Extralabel use withdrawal time: 1 day for meat and 24 hours for milk.

Horses: Clearance prior to racing: approximately 2.5 days.

Racing Commissioners International (RCI) Classification: 2

## Lincomycin Hydrochloride, Lincomycin Hydrochloride Monohydrate

lin-koe-mye'sin hye-droe-klor'ide, lin-koe-mye'sin hye-droe-klor'ide mono-hye'drate

**Trade and other names:** Lincocin and Lincomix

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Lincosamide antibiotic. Lincomycin is similar in mechanism to clindamycin. Mechanism of action is also similar to macrolides, such as erythromycin, and there may be cross-resistance among these drugs. Like the other related drugs, the site of action is the 50S ribosomal subunit. By inhibiting this ribosome, it decreases protein synthesis. In most bacteria, it is bacteriostatic. The spectrum includes primarily gram-positive bacteria and atypical bacteria such as *Mycoplasma*.

### Indications and Clinical Uses

Lincomycin has a gram-positive spectrum and has limited use for other infections. In small animals, it is used for pyoderma and other soft tissue infections caused by susceptible gram-positive bacteria. It is also active against *Mycoplasma*, *Erysipelothrix*, and *Leptospira* species. In pigs and birds, it is used primarily for treatment of infections caused by *Mycoplasma*. It is also used in pigs, added to feed and water, to control swine dysentery caused by *Brachyspira hyodysenteriae*. Although it has been injected IM in cattle and sheep for treatment of septic arthritis, laryngeal abscesses, and mastitis, this treatment is not currently recommended. Compared to lincomycin, clindamycin has better activity against anaerobic bacteria. In dogs and cats, because of availability, clindamycin is administered more often than lincomycin.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are uncommon. Lincomycin has caused vomiting and diarrhea in animals. Severe, and even fatal, enteritis can be caused from oral administration to ruminants.

#### Contraindications and Precautions

Do not administer orally to rodents, horses, ruminants, or rabbits. Oral administration to ruminants and horses can cause severe enteritis.

#### Drug Interactions

No drug interactions reported for animals.

### Instructions for Use

Action of lincomycin and clindamycin are similar enough that clindamycin can be substituted for lincomycin.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) break points for sensitive organisms are less than or equal to 0.25 mcg/mL for streptococci and less than or equal to 0.5 for other organisms.

### Formulations

- Lincomycin is available in 100-, 200-, and 500-mg tablets; 400 mg/g of powder; 16 g/40 g of soluble powder; 10-, 20-, and 50-g/lb of premix; 50-mg/mL syrup; and 25-, 100-, and 300-mg/mL solution for injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 15-25 mg/kg q12h PO.
- Pyoderma: 10 mg/kg q12h PO.

## Large Animal Dosage

### Pigs

- Swine dysentery: 250 mg per gallon of drinking water, which is approximately 8.4 mg/kg/day if given as the only source of drinking water for 5-10 days.
- *Mycoplasma* infections: 11 mg/kg q24h or 11 mg/kg q12h IM injection.

### Cattle

- Septic arthritis, mastitis, and abscesses: 5 mg/kg q24h IM for 5-7 days.
- Refractory infections: 10 mg/kg q12h IM.

### Sheep

- Septic arthritis: 5 mg/kg q24h for 3-5 days IM.

## Regulatory Information

Withdrawal time for pigs: 0, 1, 2, or 6 days, depending on product and route of administration. (For most products, allow 6 days for oral administration and 2 days for IM administration.) For extralabel use in cattle, FARAD recommends 7 days for meat and 96 hours for milk, at a dose of 5 mg/kg.

## Linezolid

lih-neh-zoe'lide

**Trade and other names:** Zyvox, Zyvoxam (Canada), and generic

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Linezolid is an antibiotic in the oxazolidinone class (synthetic drugs). Tedizolid (Sivextro) is a related drug, but has not been used in animals. Linezolid is bacteriostatic with a unique mechanism of action. It inhibits protein synthesis by binding to a site on the bacterial 23S ribosomal RNA of the 50S subunit. This prevents formation of the 70S ribosomal unit; therefore protein synthesis is inhibited. Linezolid has good penetration into cells and extracellular fluid. Urine concentrations are high enough to inhibit urinary tract pathogens. In dogs, the oral absorption is almost 100%, and the half-life is slightly faster than humans. Linezolid does not undergo hepatic P450 metabolism, and one third of the total clearance relies on the kidneys.

## Indications and Clinical Uses

Linezolid is active against streptococci and staphylococci and is indicated for treatment of infections that have become resistant to other drugs, particularly when there is resistance to the beta-lactam antibiotics (penicillins, ampicillin derivatives, and cephalosporins). It is not indicated for gram-negative infections. Linezolid is indicated for

treatment of methicillin-resistant and oxacillin-resistant strains of *Staphylococcus* (e.g., methicillin-resistant *S. aureus* [MRSA] and methicillin-resistant *S. pseudintermedius* [MRSP]) and drug-resistant *Enterococcus* spp. Because of the high cost of linezolid, it is not used for routine infections.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects include diarrhea and nausea. Rarely, anemia and leukopenia have been observed in people. The risk of bone marrow suppression is most evident after 2 weeks of treatment. Longer treatment courses should be accompanied by periodic CBC measurements.

#### Contraindications and Precautions

No contraindications reported.

#### Drug Interactions

Linezolid is a type A monoamine oxidase inhibitor (MAOI). Possible interactions occur with serotonin reuptake inhibitors such as fluoxetine and selegiline to produce serotonin syndrome. Interactions are also possible if administered with adrenergic drugs such as phenylpropanolamine. However, this effect has not been reported for animals. Linezolid is not expected to affect metabolism of other drugs. Rifampin may decrease plasma concentrations. Intravenous formulation is physically incompatible with other drugs in IV line. If administered with other drugs intravenously, flush out administration line first.

### Instructions for Use

Linezolid is reserved for infections that are resistant to other drugs, such as *Enterococcus* spp., or methicillin-resistant *Staphylococcus* infections.

### Patient Monitoring and Laboratory Tests

Choice of drug should be selected on the basis of susceptibility monitoring. CLSI lists the break point for susceptibility as less than or equal to 4.0 mcg/mL for *Staphylococcus* and less than or equal to 2.0 mcg/mL for *Enterococcus*. Ideal plasma drug concentrations are 2-7 mcg/mL.

### Formulations

- Linezolid is available in 400- and 600-mg tablets, 20-mg/mL oral suspension powder, and 2-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with other drugs. Oral suspension is stable for 21 days after reconstitution at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 10 mg/kg q12h PO or IV. (Use every 8 hours for serious infections and every 12 hours for less life-threatening infections.)

### Large Animal Dosage

- No large animal dose is available.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Liothyronine Sodium

lye-oh-thye'roe-neen soe'dee-um

**Trade and other names:** Cytomel

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Thyroid supplement. Liothyronine is equivalent to  $T_3$ .  $T_3$  is more active than  $T_4$ , but ordinarily  $T_4$  is converted in animals to the active form of  $T_3$ .

### Indications and Clinical Uses

Liothyronine is used for similar indications as levothyroxine ( $T_4$ ), except that in this instance, the active  $T_3$  hormone is administered. It may be indicated in cases in which there is failure to convert  $T_4$  to the active  $T_3$  hormone. In most cases, it is preferred to administer levothyroxine instead of liothyronine.

#### Precautionary Information

##### Adverse Reactions and Side Effects

Adverse effects have not been reported.

##### Contraindications and Precautions

No contraindications reported.

##### Drug Interactions

No drug interactions reported for animals.

### Instructions for Use

Doses of liothyronine should be adjusted on the basis of monitoring  $T_3$  concentrations in patients. It is rarely necessary to administer  $T_3$  alone for treatment of hypothyroidism. In most patients, drugs that contain  $T_4$  should be used (e.g., levothyroxine). Liothyronine has been used as a diagnostic test for cats.

### Patient Monitoring and Laboratory Tests

Monitor serum  $T_3$  concentrations. Used for  $T_3$ -suppressing test in cats.

### Formulations

- Liothyronine is available in 5-, 25-, and 50-mcg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 4.4 mcg/kg q8h PO.
- $T_3$  suppression test in cats: Collect presample for  $T_4$  and  $T_3$ , administer 25 mcg q8h for 7 doses, and then collect postsamples for  $T_3$  and  $T_4$  after last dose.

### Large Animal Dosage

- No large animal dose is available.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).



## Lisinopril

lye-sin'oh-pril

**Trade and other names:** Prinivil and Zestril

**Functional classification:** Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

### Pharmacology and Mechanism of Action

Like other ACE inhibitors, lisinopril inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and will also stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The ability of aldosterone to cause sodium and water retention contributes to congestion. Lisinopril, like other ACE inhibitors, will cause vasodilation and decrease aldosterone-induced congestion. Lisinopril also contributes to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins. Like other ACE inhibitors, lisinopril can reduce renal hypertension and improve renal perfusion, decrease glomerular pressure, and lead to improvement in some patients with renal disease.

### Indications and Clinical Uses

Lisinopril, like other ACE inhibitors, is used to treat hypertension and congestive heart failure (CHF). Enalapril and benazepril have been used more often in animals. Other uses may include primary hypertension. Lisinopril also may be used to treat some forms of renal disease in animals. When glomerular filtration pressures are high, lisinopril may improve some patients with renal disease, but effects on survival have not been established.

### Precautionary Information

#### Adverse Reactions and Side Effects

Like other ACE inhibitors, it may cause azotemia in some patients. Carefully monitor patients receiving high doses of diuretics.

#### Contraindications and Precautions

Discontinue ACE inhibitors in pregnant animals; they cross the placenta and have caused fetal malformations and death of the fetus.

#### Drug Interactions

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs may decrease vasodilating effects.

### Instructions for Use

Clinical studies using lisinopril in animals have not been reported. The doses and clinical use have been extrapolated from human studies, or limited anecdotal experience in animals.

### Patient Monitoring and Laboratory Tests

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

### Formulations

- Lisinopril is available in 2.5-, 5-, 10-, 20-, and 40-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Lisinopril has been mixed with syrup for oral administration and found to be stable for 30 days at either room temperature or refrigerated.

## Small Animal Dosage

### Dogs

- 0.5 mg/kg q24h PO.

### Cats

- No dose established.

## Large Animal Dosage

- No large animal dose is available.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Lithium Carbonate

lih'thee-um kar'boe-nate

**Trade and other names:** Lithotabs

**Functional classification:** Immunostimulant

## Pharmacology and Mechanism of Action

Lithium stimulates granulopoiesis and elevates the neutrophil pool in animals. It also affects the CNS because it affects the balance of CNS neurotransmitters.

## Indications and Clinical Uses

In people, lithium is used for treatment of depression. It has not been used for this purpose in animals. It has also been used experimentally to increase neutrophil counts following cancer therapy and to prevent cytotoxicity caused from anticancer drugs.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects include nephrogenic diabetes insipidus, ptyalism, lethargy, and seizures. In people, cardiovascular problems, drowsiness, and diarrhea are among the adverse effects.

### Contraindications and Precautions

Not recommended in cats.

### Drug Interactions

No drug interactions are reported.

## Instructions for Use

Use in animals is uncommon, and little dosing information is available.

## Patient Monitoring and Laboratory Tests

Monitor neutrophil count.

## Formulations

- Lithium is available in 150-, 300-, and 600-mg capsules; 300-mg tablets; and 300-mg/5 mL syrup.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- 10 mg/kg q12h PO.

**Cats**

- Not recommended.

**Large Animal Dosage**

- No large animal dose is available.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Lomustine**

loe-mus'teen

**Trade and other names:** CeeNU and CCNU**Functional classification:** Anticancer agent**Pharmacology and Mechanism of Action**

Anticancer agent. It is one of two nitrosoureas used: lomustine (1-[2-chloroethyl]-3-cyclohexyl-1-chloroethylnitrosourea), known by the abbreviation of CCNU, and carmustine (1,3-bis-2-chloroethyl-1-nitrosourea), known by the abbreviation BCNU. Both of the nitrosoureas are metabolized spontaneously to alkylating and carbamylating compounds. Lomustine transfers the chloroethyl group of the nitrosourea to the O-6 methyl of guanine on DNA. This causes interstrand and intrastrand cross-linking of DNA, which inactivates DNA synthesis and cell death. Therefore, bifunctional interstrand cross-links are responsible for the cytotoxicity of nitrosoureas. Oral absorption and high membrane penetration are attributed to high lipophilicity. Because oral absorption is high, lomustine can be administered effectively as oral tablets. After absorption, lomustine is metabolized to antitumor metabolites. Both the parent drug and the metabolites are lipid soluble. The CNS penetration of lomustine has been determined from the plasma/cerebrospinal fluid (CSF) ratio, which is 1:3.

**Indications and Clinical Uses**

Lomustine (CCNU) is used to treat tumors of the CNS (brain tumors), round cell tumors, mast cell tumors, sarcomas, and lymphoma in dogs and cats. It has occasionally been used to treat other forms of cancer. Lomustine has been used more often than carmustine. It has been well tolerated in cats. At doses of approximately 10 mg per cat every 3 weeks, it produced minimal myelosuppression.

**Precautionary Information****Adverse Reactions and Side Effects**

Bone marrow effects are the most serious. In people, lomustine has a delayed nadir of bone marrow toxicity, which is as long as 4-6 weeks with slow recovery, but in dogs, the nadir of bone marrow effects generally is seen 6-7 days after dosing. Maximum tolerated dose in dogs is 90 mg/m<sup>2</sup>. At higher doses (100 mg/m<sup>2</sup>), myelosuppression has been reported. Thrombocytopenia also has been reported

from lomustine administration as a cumulative effect. If severe neutropenia is observed in dogs, lower dose to 40-50 mg/m<sup>2</sup>.

In cats, neutropenia is the most dose-limiting effect of treatment. Thrombocytopenia also is possible. Cats resemble people in that bone marrow nadir of toxicity occurs at 3-4 weeks. Nitrosoureas also can be toxic to the rapidly dividing cells of mucosa.

In people, nitrosoureas also have caused pulmonary fibrosis and hepatotoxicity. Hepatotoxicity may be a delayed reaction. In people, carmustine (BCNU) has been associated with a higher rate of hepatic injury than lomustine. The hepatic injury from lomustine observed in dogs has been irreversible.

### Contraindications and Precautions

Consider risks to bone marrow with use in small animals.

### Drug Interactions

Use with caution with any drugs that may cause bone marrow suppression.

## Instructions for Use

The nitrosourea drugs are used to treat CNS tumors and other forms of cancer. Protocols used in small animals are different from those given to people, which are as much as 150-200 mg/m<sup>2</sup>. Oral treatment should be given on an empty stomach if possible.

## Patient Monitoring and Laboratory Tests

Monitor CBC and liver enzymes in treated patients.

## Formulations

- Lomustine is available in 10-, 40-, and 100-mg capsules.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 70-90 mg/m<sup>2</sup> q4wk PO.
- Lymphoma: 60 mg/m<sup>2</sup> q4wk, for four treatments.
- Brain tumors: 60-80 mg/m<sup>2</sup> q6-8wk PO.
- Where liver injury is a concern in dogs, use a lower and safer dose of 40 mg/m<sup>2</sup>.

### Cats

- 50-60 mg/m<sup>2</sup> q3-6wk PO. Alternatively, administer 10-20 mg/cat q3-6wk.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Do not administer to animals that produce food.

## Loperamide Hydrochloride

loe-pare'ah-mide hye-droe-klor'ide

**Trade and other names:** Imodium and generic brands

**Functional classification:** Analgesic, opioid

## Pharmacology and Mechanism of Action

Opiate agonist. Like other opiates, loperamide acts on the mu-opiate receptors of the GI tract. It decreases propulsive intestinal contractions and increases segmentation (an overall constipating effect). It also increases the tone of GI sphincters. In addition to affecting motility, opiates have an antisecretory effect and stimulate absorption of fluid, electrolytes, and glucose. Their effects on secretory diarrhea are probably related to inhibition of calcium influx and decreased calmodulin activity. Action of loperamide is limited to the intestine. Central nervous system effects do not occur because it does not cross the blood–brain barrier.

## Indications and Clinical Uses

Loperamide is used for symptomatic treatment of acute nonspecific diarrhea. It has been administered orally to dogs and cats. Long-term use is discouraged because it may lead to constipation. It has been administered to large animals, but this is not recommended.

### Precautionary Information

#### Adverse Reactions and Side Effects

Loperamide can cause severe constipation with repeated use. In some dogs that have a mutation in the ABCB1 gene (previously known as the MDR gene), they may lack P-glycoprotein in the blood–brain barrier. In these susceptible animals, loperamide will cross the blood–brain barrier and cause profound sedation. Such cases may be reversed with naloxone. Dogs most susceptible include collie breeds, Australian shepherds, Old English sheepdogs, longhaired whippets, and Shetland sheepdogs.

#### Contraindications and Precautions

Small dogs and collie-type dogs may be at higher risk of adverse effects.

#### Drug Interactions

Do not administer with drugs that may act as MDRI (p-glycoprotein) membrane inhibitors, such as ketoconazole. (Other inhibitors are listed in Appendix J.) These inhibitors may increase blood–brain barrier penetration and cause depression.

## Instructions for Use

Doses are based primarily on empiricism or extrapolation of human doses. Clinical studies have not been performed in animals.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Loperamide is available in 2-mg tablets, 2-mg capsules, and 0.2-mg/mL oral liquid (over the counter [OTC]).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Loperamide is slightly soluble in water but only at low pH. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 0.12 mg/kg q8-12h PO.

### Cats

- 0.08-0.16 mg/kg q12h PO.

## Large Animal Dosage

- No large animal doses have been reported. If administered to horses or ruminants, it may induce problems associated with decreased intestinal motility.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Lorazepam

lor-ay'zeh-pam

**Trade and other names:** Ativan and generic brands

**Functional classification:** Anticonvulsant

## Pharmacology and Mechanism of Action

Benzodiazepine. Central-acting CNS depressant, with action similar to diazepam. Mechanism of action appears to be via potentiation of gamma aminobutyric acid (GABA) receptor-mediated effects in CNS. In animals, lorazepam does not undergo extensive hepatic metabolism, but it is glucuronidated before excretion. In dogs, lorazepam had a half-life of 0.9 hours, with systemic clearance less than half that of diazepam. Oral absorption is 60%. Therefore the oral formulation may be suitable in dogs for some conditions.

## Indications and Clinical Uses

Lorazepam, as a benzodiazepine, may be considered for anxiety disorders in animals, but it has not been used as commonly as other drugs such as diazepam, alprazolam, or midazolam. Lorazepam also is effective for treating seizures, but it is not used as often in animals as other anticonvulsants. In controlled studies, it has been equally as effective as an anticonvulsant as diazepam in dogs.

## Precautionary Information

### Adverse Reactions and Side Effects

Sedation is the most common side effect. Lorazepam causes polyphagia. Some animals may experience paradoxical excitement. Chronic administration may lead to dependence and a withdrawal syndrome if discontinued.

### Contraindications and Precautions

Oral administration of another benzodiazepine, diazepam, has caused idiosyncratic liver injury in cats, but this is unlikely for lorazepam because of a different route of metabolism.

### Drug Interactions

Use cautiously with other drugs that may cause sedation. Do not mix with buprenorphine.

## Instructions for Use

Doses based on empiricism. There have been no clinical trials in veterinary medicine, although it is expected to produce effects similar to other benzodiazepines. For IV use, dilute 50/50 with 0.9% saline or 5% dextrose prior to use.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations Available**

- Lorazepam is available in 0.5-, 1-, and 2-mg tablets and 2- and 4-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Lorazepam is practically insoluble in water. It is slightly soluble in some infusion solutions (e.g., 0.054 mg/mL in 5% dextrose). Solutions should be discarded if they turn a dark color.

**Small Animal Dosage****Dogs**

- 0.05 mg/kg q12h PO.
- Seizures: 0.2 mg/kg IV. Repeat every 3-4 hours for seizure control if necessary; or 0.2 mg/kg bolus, followed by 0.2-0.4 mg/kg/hour IV CRI.

**Cats**

- 0.05 mg/kg q12-24h PO.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

Do not administer to animals intended for food.

Schedule IV controlled drug

RCI Classification: 2

**Losartan**

loe-zar'tan

**Trade and other names:** Cozaar

**Functional classification:** Vasodilator

**Pharmacology and Mechanism of Action**

Vasodilator, angiotensin II receptor blocker (ARB). It has high affinity and selectivity for the AT<sub>1</sub> receptor. The action is similar to that of ACE inhibitors, except that it directly blocks the receptor, rather than inhibits synthesis of angiotensin II. Angiotensin II receptor blockers have the advantage of being less likely to induce hyperkalemia and are more easily tolerated in people. Losartan and other ARBs have been used in people who cannot tolerate ACE inhibitors.

In people, losartan is metabolized to the active carboxylic acid metabolite (E-3174), which is 10-40 times more potent than the parent drug and with a longer half-life than the parent drug, and is believed to be responsible for most clinical effects. In dogs, oral absorption of the parent drug is low (23%-33%) and half-life is short (1.8-2.5 hours) with high clearance producing a short duration of activity. Dogs do not form the E-3174 metabolite, which is responsible for therapeutic effects in people. Because of this difference, dogs may require higher doses than used in people to produce therapeutic effects.

## Indications and Clinical Uses

In dogs, it is reported that they do not convert losartan to the active metabolite, and therefore it has little activity in dogs. However, a related drug, irbesartan (30 mg/kg q12h), has been shown to block angiotensin II receptors. Telmisartan has a longer half-life and is more lipophilic and may be more effective in dogs.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse reactions have been reported in animals. In people, hypotension may occur.

#### Contraindications and Precautions

No specific contraindications have been reported for animals. Do not use in pregnant animals.

#### Drug Interactions

Combined use of ARB and ACE inhibitor may increase risk of kidney injury.

## Instructions for Use

In dogs, losartan is not converted to the active metabolite. Therefore it has little bioactivity (*J Pharmacol Exp Ther*, 268:1199-1205, 1999) and high doses will be needed to produce clinical effects. It is suggested instead to consider irbesartan at a dose of 30 mg/kg q12h PO.

## Patient Monitoring and Laboratory Tests

Monitor blood pressure in treated animals.

## Formulations

- Losartan is available in 25-, 50-, and 100-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 0.125 mg/kg per day in azotemic patients; 0.5 mg/kg/day in nonazotemic patients.

### Cats

- No dose established.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 3

## Lufenuron

loo-fen'yoo-rah-n

**Trade and other names:** Program

**Functional classification:** Antiparasitic



## Pharmacology and Mechanism of Action

Antiparasitic. Lufenuron is a benzoylurea insecticide. This class of insecticides was previously used on fruits to decrease damage by insects. Lufenuron (Program) has been used for prevention of flea infections in dogs and cats because it inhibits chitin synthesis. For this use, it has been given to dogs at a dose of 10 mg/kg every 30 days and to cats at a dose of 30 mg/kg every 30 days. It may also have some inhibition on fungal cell membranes because it inhibits the cell wall of fungi, which contain chitin, and other complex polysaccharides. Because of this property on fungal cell membranes, there has been interest in using lufenuron to treat dermatophytes in small animals. However, proven efficacy has been controversial. Well-controlled studies have not confirmed consistent efficacy for treating dermatophytes in animals.

## Indications and Clinical Uses

Lufenuron is used to control flea infestations by preventing hatching of eggs. It has been used as part of flea control, often with other drugs that kill adult fleas. Lufenuron has been combined with milbemycin in formulations for small animals, and additional details may be found in the section on milbemycin. There are clinical reports of the use of lufenuron for treating dermatophyte infections in small animals—particularly cats—at high doses of 80-100 mg/kg orally. However, endorsement of this use has diminished, and dermatologists have disputed the efficacy and have observed a high incidence of recurrence. In horses, lufenuron was not absorbed orally and is not effective for treating fungal infections. It does not have any in vitro effect on *Aspergillus fumigatus* or *Coccidioides immitis*.

### Precautionary Information

#### Adverse Reactions and Side Effects

Refer to the section on lufenuron or milbemycin for details.

#### Contraindications and Precautions

No contraindications are reported for animals. Some animals may be sensitive to milbemycin, and additional details are found in that section.

#### Drug Interactions

No drug interactions reported for animals, except those that may pertain to milbemycin.

## Instructions for Use

Lufenuron is a highly lipophilic drug and is absorbed best with a meal. If cats have free access to their food, withhold their food until such time that a meal will be consumed readily before administering the lufenuron oral dose. Lufenuron may control flea development with administration once every 30 days in animals.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Lufenuron is available in 45-, 90-, 135-, 204.9-, and 409.8-mg tablets and 135- and 270-mg suspension per unit pack.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- Flea control: 10 mg/kg q30d PO.
- Dermatophytes: 80 mg/kg, every 2 weeks, PO (efficacy questionable).

### Cats

- Flea control: 30 mg/kg q30d PO or injection of 10 mg/kg SQ every 6 months.
- Dermatophytes: 80 mg/kg; 100 mg/kg PO is the minimum dose for treating cats in a cattery. These doses should be repeated initially after the first 2 weeks and possibly once per month in animals that may be reexposed (efficacy questionable).

## Large Animal Dosage

### Horses

- Not effective.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Lufenuron Milbemycin Oxime

loo-fen'yoo-rahn + mil-beh-mye'sin oks'eem

**Trade and other names:** Sentinel tablets and Flavor Tabs

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Combination of two antiparasitic drugs. Refer to sections on lufenuron or milbemycin for details.

## Indications and Clinical Uses

Lufenuron + milbemycin is used to protect against fleas, heartworms, roundworms, hookworms, and whipworms.

### Precautionary Information

#### Adverse Reactions and Side Effects

There is a high margin of safety at doses used for flea control or treatment of dermatophytes. Adverse effects have not been reported. Lufenuron appears to be relatively safe in pregnant and young animals.

#### Contraindications and Precautions

No contraindications are reported for animals.

#### Drug Interactions

No drug interactions are reported for animals.

## Instructions for Use

See section on lufenuron or [milbemycin](#) for details.

## Patient Monitoring and Laboratory Tests

Monitor for heartworm status in dogs before initiating treatment with milbemycin.

### Formulations

- The milbemycin/lufenuron ratio is as follows: 2.3/46-mg tablets and 5.75/115-, 11.5/230-, and 23/460-mg Flavor Tabs.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- Administer one tablet every 30 days based on tablet size and weight range listed in product label.
- Each tablet is formulated for the size of the dog.

#### Cats

- No dose is reported.

### Large Animal Dosage

- No large animal doses have been reported.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Lysine (L-Lysine)

lye' seen

**Trade and other names:** Enisyl-F

**Functional classification:** Antiviral

### Pharmacology and Mechanism of Action

Lysine is an amino acid–based supplement for treating feline herpes virus type 1 (FHV-1). It acts by antagonism of the growth-promoting effect of arginine, which is an essential amino acid of FHV-1.

### Indications and Clinical Uses

Lysine is a nutritional supplement for treating FHV-1 in cats. It is intended to reduce viral shedding in infected cats and may improve some clinical signs associated with FHV. However, it has questionable efficacy for treatment of upper respiratory infections in cats. Dietary lysine did not control upper respiratory or ocular infection in cats studied in a shelter environment and actually led to an increase in severity of some infections. For this reason, routine use for viral infections in cats should be reevaluated.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse effects have been reported in cats.

#### Contraindications and Precautions

No contraindications have been reported.

#### Drug Interactions

No drug interactions have been reported for animals.

### Instructions for Use

L-Lysine monohydrate can be supplied as a powder and mixed with a small amount of food.

### Patient Monitoring and Laboratory Tests

Monitor patient's CBC during treatment.

### Formulations

Paste (Enisyl-F) is distributed in syringes in which each mark on the syringe represents 1 mL (250 mg/mL). It has also been available for cats as a metered-dose pump to add to food, 100-g powder (to be mixed with food), 5-oz oral gel (Viralys), 600-mL oral paste, and flavored treats.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Cats

- 400 mg/cat/day PO, daily supplement added to cat food.
- Paste formulation: 1-2 mL to adult cats and 1 mL to kittens.

### Large Animal Dosage

- No large animal doses have been reported.

### Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

## Magnesium Citrate

**Trade and other names:** Citroma, CitroNesia, and Citro-Mag (Canada)

**Functional classification:** Laxative

### Pharmacology and Mechanism of Action

Saline cathartic. Acts to draw water into the small intestine via an osmotic effect. Fluid accumulation produces distension, which promotes bowel evacuation.

### Indications and Clinical Uses

Magnesium citrate is administered orally for constipation and bowel evacuation prior to certain procedures. It also may be used to promote intestinal clearance of an ingested toxin. It is prompt in its cathartic action. In the formulation Pronefra (in combination with calcium carbonate) it is used as a phosphate binder to patients with kidney disease.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. However, fluid and electrolyte loss can occur with overuse.

#### Contraindications and Precautions

Magnesium accumulation may occur in patients with renal impairment. Cathartics containing magnesium decrease oral absorption of ciprofloxacin and other fluoroquinolones.

#### Drug Interactions

No drug interactions have been reported for animals. However, it may increase clearance of some drugs administered orally.

### Instructions for Use

Magnesium citrate is commonly used to evacuate the bowel prior to surgery or diagnostic procedures. Doses are empirical and extrapolated from other species. Onset of action is rapid.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. However, monitor magnesium concentrations in patients if repeated treatments or high doses are administered.

### Formulations

- Magnesium citrate is available in a 6% oral suspension. The formulation Pronefra also is available as calcium carbonate and magnesium carbonate. It is an oral syrup that may be administered as a phosphate binder in cats and dogs. Pronefra is a palatable liquid suspension with poultry liver flavoring.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 2-4 mL/kg/day PO. For the Pronefra product (in combination with calcium carbonate) administer twice daily at meal time. 1 mL per cat, or 1 mL per dog, twice daily, PO. Preferably at meal time.

## Large Animal Dosage

### Horses and Cattle

- 2-4 mL/kg once PO.

## Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

## Magnesium Hydroxide

**Trade and other names:** Milk of Magnesia, Carmilax, and Magnalax

**Functional classification:** Laxative

## Pharmacology and Mechanism of Action

Saline cathartic. Magnesium hydroxide acts to draw water into the small intestine via an osmotic effect. Fluid accumulation produces distension, which promotes bowel evacuation.

## Indications and Clinical Uses

Magnesium hydroxide is used for constipation and bowel evacuation prior to certain procedures. It is commonly used to evacuate the bowel prior to surgery or diagnostic procedures. Onset of action is rapid. Magnesium hydroxide also is used as an oral antacid to neutralize stomach acid. In large animals, it is used as an antacid and mild cathartic. In cattle, approximately 1 g/kg as a single dose significantly increases rumen pH and decreases rumen microbial activity.

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## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. However, fluid and electrolyte loss can occur with overuse.

### Contraindications and Precautions

Magnesium accumulation may occur in patients with renal impairment.

### Drug Interactions

Cathartics containing magnesium decrease oral absorption of ciprofloxacin and other fluoroquinolones.

## Instructions for Use

Administer to patients only if they are properly hydrated.

## Patient Monitoring and Laboratory Tests

Monitor electrolytes with chronic use.

## Formulations

- Magnesium hydroxide is available as an oral liquid 400 mg/5 mL, or 400 mg per teaspoon (Milk of Magnesia) over the counter (OTC). It is also available as a 27- or 90-g bolus for cattle and sheep and as a powder 310-360 g/lb (approximately 745 g/kg). As a powder, 1 pound of powder is equivalent to 1 gallon of Milk of Magnesia, and three 27-g boluses are equal to 1 quart of Milk of Magnesia.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- Antacid: 5-10 mL/dog q4-6h PO.
- Cathartic: 15-50 mL/dog q24h PO.

### Cats

- Antacid: 5-10 mL/cat q4-6h PO.
- Cathartic: 2-6 mL/cat q24h.

## Large Animal Dosage

### Sheep and Cattle

- 1 g/kg or 1 bolus per 27 kg (60 pounds) PO, once (3-4 boluses for adult cattle).
- For the powder, mix 1 lb with 1 gallon water and administer 500 mL/45 kg (500 mL per 100 pounds). For the product Polyox, administer 180 mL for animals less than 225 kg and 360 mL if greater than 225 kg body weight.

## Regulatory Information

Withdrawal time for animals intended for food: 12-24 hours (milk) depending on the product.

## Magnesium Sulfate

**Trade and other names:** Epsom salts

**Functional classification:** Laxative, antiarrhythmic

## Pharmacology and Mechanism of Action

Saline cathartic, antiarrhythmic, and used to treat magnesium deficiency. When administered orally, magnesium sulfate acts to draw water into the small intestine via an osmotic effect. Fluid accumulation produces distension, which promotes bowel evacuation. Magnesium sulfate is administered intravenously to patients who are magnesium deficient and is used as an antiarrhythmic. When used as an antiarrhythmic, it serves as a source of magnesium for treating refractory arrhythmias because in animals with hypomagnesemia, it acts as a cofactor for the Na/K ATPase pump. It also may block calcium channels.

## Indications and Clinical Uses

Magnesium sulfate is used for constipation and bowel evacuation prior to certain procedures. An injectable solution of magnesium sulfate is used to treat magnesium deficiency and refractory arrhythmias in patients who are critically ill. (Magnesium chloride also has been used.) A dose of 1-2 mEq/kg of magnesium sulfate produced plasma concentrations of 8.5-12.2 mEq/L, and can increase heart rate, inotropy, and cardiac output.

In horses, magnesium sulfate is administered for ventricular tachycardia that is not responsive to other drugs. In cattle, magnesium sulfate is used to treat hypomagnesemia, especially in dairy cattle.

## Precautionary Information

### Adverse Reactions and Side Effects

High doses may cause muscle weakness and respiratory paralysis. Mild signs of toxicity during magnesium treatment include vomiting, diarrhea, hypotension, and weakness. With repeated administration, fluid and electrolyte loss can occur with overuse. When treating arrhythmias, it has been administered at doses of 0.1-0.2 mEq/kg safely. At doses higher than 1.0 mmol/kg (2.0 mEq/kg), deterioration of hemodynamic parameters may occur.

### Contraindications and Precautions

Magnesium accumulation may occur in patients with renal impairment.

### Drug Interactions

Magnesium sulfate can be added to fluids containing sodium chloride (0.9%), dextrose (5%), and water. Do not mix with calcium-, bicarbonate-, and lactate-containing solutions. Incompatible with magnesium salt solutions. Cathartics containing magnesium decrease oral absorption of ciprofloxacin and other fluoroquinolones. Magnesium sulfate is incompatible with alkaline solutions. Some metal ions (e.g., calcium) may form insoluble sulfates.

### Instructions for Use

When used as a laxative, magnesium sulfate is administered for its prompt action to evacuate the bowel prior to surgery or diagnostic procedures. Onset of action is rapid. For use in cattle (hypomagnesemia), an initial dose can be administered IV, followed by an SQ dose to produce a sustained effect. Monitor animals for hypocalcemia, which can occur simultaneously.

### Patient Monitoring and Laboratory Tests

When treating magnesium deficiency or arrhythmias with IV magnesium sulfate, monitor the electrocardiogram (ECG) during infusion and observe for bradycardia, QT interval prolongation, and QRS complex widening. Monitor magnesium, potassium, sodium, chloride, and calcium concentrations during treatment. Normal magnesium concentrations in animals are 1.32-2.46 mEq/L. Many cattle also have hypocalcemia.

### Formulations

- Magnesium sulfate is available as solid crystals in generic preparations. Solution for injection is 12.5%-50%. When administering IV, dilute to concentration below 20% using sodium chloride (0.9%), 5% dextrose, or water. Intravenous and subcutaneous solutions for cattle are usually 1.5-4 g/L.

### Stability and Storage

Crystals are stable if stored in a dry container. Store injectable solutions at room temperature, in a tightly sealed vial, protected from light.

### Small Animal Dosage

#### Dogs

- 1-2 mEq/kg/day PO, equivalent to 0.5-1.0 mmol/kg PO (or 8-25 g/dog q24h PO).

#### Cats

- 2-5 g/cat q24h PO.

#### Dogs and Cats

- Intravenous dose for magnesium deficiency or arrhythmias: 0.2-0.3 mEq/kg (0.1-0.15 mmol/kg) IV at a rate of 0.12 mEq/kg/min (0.06 mmol/kg/min).
- Constant-rate infusion (CRI) for treating arrhythmias or ongoing deficiency: 0.2-1.0 mEq/kg/day IV (0.1-0.5 mmol/kg/day).
- Use during fluid therapy: Supplement fluid solutions with 0.75-1 mEq/kg/day.

### Large Animal Dosage

#### Cattle

- 2-3 g per cow IV over 10 minutes. This may be followed by 200-400 mL per cow of 25% magnesium sulfate SQ to supply 50-100 g per cow.



**Horses**

- 1 g/horse q12-24h PO or 2-4 mg/kg IV. For ventricular tachycardia, an infusion of 1 g/min, up to a maximum of 25 g, can be administered intravenously.

**Regulatory Information**

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

**Mannitol**

man'ih-tole

**Trade and other names:** Osmitol

**Functional classification:** Diuretic

**Pharmacology and Mechanism of Action**

Hyperosmotic diuretic. Mannitol occurs naturally as a sugar in fruits and vegetables. As an osmotic diuretic, mannitol is freely filtered by the glomerulus, but it is not reabsorbed by the renal tubule. Therefore it increases osmolality of the urine. The osmotic effect inhibits reabsorption of fluid from the renal tubules, and this produces a natriuretic effect and strong diuresis. Reabsorption of sodium chloride and solutes also is inhibited. Mannitol, compared to other diuretic drugs, produces a more profound diuretic effect, which can potentially cause excessive fluid loss in a patient. After IV administration, mannitol increases the plasma osmolality, which draws fluid from tissues to plasma, which is helpful for treating tissue edema. It reduces intracranial pressure for treating cerebral edema. It is also used as an antiglaucoma agent because it lowers intraocular pressure when administered intravenously.

**Indications and Clinical Uses**

Mannitol is administered intravenously for treatment of cerebral edema, acute glaucoma, and conditions associated with tissue edema. Mannitol also has been used to promote urinary excretion of certain toxins and in the management of anuric or oliguric renal failure.

**Precautionary Information****Adverse Reactions and Side Effects**

Mannitol produces a profound diuresis and can cause significant fluid loss and electrolyte imbalance. An administration rate that is too rapid may expand the extracellular volume excessively.

**Contraindications and Precautions**

Do not use in patients who are dehydrated. Use cautiously when intracranial bleeding is suspected because it may increase bleeding. (This effect is controversial when dealing with intracranial hemorrhage.)

**Drug Interactions**

Do not administer simultaneously with blood replacement. If blood is administered simultaneously, sodium chloride must be added to each liter of mannitol (20 mEq/L). Mannitol may increase renal clearance of some drugs.

## Instructions for Use

Use only in animals in which fluid and electrolyte balance can be monitored.

## Patient Monitoring and Laboratory Tests

Monitor hydration and electrolyte balance in treated animals. Monitor intraocular pressure when treating acute glaucoma.

## Formulations

- Mannitol is available in a 5%, 10%, 15%, 20%, and 25% solution for injection. The 25% solution is equivalent to 1 g in 4-mL vials.

## Stability and Storage

Once solutions are prepared, discard unused portions. If solutions are chilled, crystals may form.

## Small Animal Dosage

### Dogs

- Diuretic: 1 g/kg of 5%-25% solution IV to maintain urine flow.
- Fluid expansion: 0.5-2 g/kg IV (or 0.1 g/kg/hr).
- Glaucoma or central nervous system (CNS) edema: 0.25-2 g/kg of 15%-25% solution over 30-60 min IV (repeat in 6 hours if necessary).

### Cats

- Fluid expansion: 0.5 g/kg to 0.8 g/kg IV over 5 minutes, followed by CRI of 1 mg/kg/min.

## Large Animal Dosage

- 0.25-1 g/kg (20% solution) IV administered over 1 hour.
- Foals: 0.25-1 g/kg IV administered as 20% solution over 15-20 minutes.

## Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

## Marbofloxacin

mar-boe-floks'ah-sin

**Trade and other names:** Zeniquin and Marbocyl (European name)

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Fluoroquinolone antimicrobial. Marbofloxacin acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. Marbofloxacin is a bactericidal with a broad spectrum of activity. Susceptible bacteria include *Staphylococcus* spp., *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*, and *Pasteurella* species. *Pseudomonas aeruginosa* is moderately susceptible but requires higher concentrations. Some methicillin-resistant *Staphylococcus* species also may be resistant to fluoroquinolones. Marbofloxacin has poor activity against streptococci and anaerobic bacteria.

## Indications and Clinical Uses

Marbofloxacin, like other fluoroquinolones, is used to treat susceptible bacteria in a variety of species. It is approved for use in dogs and cats in the United States, and in other species outside the U.S. Infections treated with marbofloxacin include skin and

soft tissue infections, bone infections, urinary tract infections (UTIs), pneumonia, and infections caused by intracellular organisms. Marbofloxacin has been effective for some blood-borne pathogens such as *Mycoplasma haemofelis* in cats at a dose of 2.75 mg/kg q24h PO for 14 days. Marbofloxacin also has been used in horses to treat infections caused by susceptible bacteria. In dogs, the half-life is 7-9 hours, but it has been longer in some studies. In horses, the half-life has varied from 4.7-7.6 hours, depending on the study. Volume of distribution in these species is 1.2-2 L/kg. Oral absorption is close to 100% in small animals and approximately 60% in horses. In cattle the half-life is 5-9 hours in calves and 4-7 hours in ruminants. In preruminant calves oral absorption is approximately 100%. In sows the half-life is 8-10 hours and oral absorption is 80%. In young pigs the half-life is 13 hours. In calves, it has been used to treat respiratory infections (bovine respiratory disease [BRD]) at 2 mg/kg for 3-5 days, or a single dose administered once at 8-10 mg/kg (see regulatory restrictions). In sows it is used to treat Mastitis-Metritis-Agalactia (MMA) syndrome. In pigs, doses of 2 mg/kg and higher reached the therapeutic targets for swine respiratory disease pathogens.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

High concentrations may cause CNS toxicity. Like other fluoroquinolones, it may cause some nausea, vomiting, and diarrhea at high doses. When administered intravenously to anesthetized patients, it did not alter cardiovascular parameters. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4-28 weeks of age. Large, rapidly growing dogs are the most susceptible. Marbofloxacin at a dose of twice the upper limit caused articular damage in dogs that were 4-5 months old. In cats 8 months old at doses of 17 and 28 mg/kg for 42 days, articular cartilage injury was observed. Blindness in cats has been reported from some quinolones such as enrofloxacin and nalidixic acid. There are no known clinical reports of this reaction with marbofloxacin, and toxicity studies by the manufacturer showed that it did not cause ocular lesions or vision problems in cats. At doses of 17 mg/kg and 28 mg/kg (three times and five times the upper limit of dosing), it did not produce ocular changes. Marbofloxacin has been administered to horses orally without producing adverse effects in the gastrointestinal tract.

#### **Contraindications and Precautions**

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures.

#### **Drug Interactions**

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur. Marbofloxacin may be administered with other antibiotics and anesthetic agents without evidence of drug interaction.

### **Instructions for Use**

At the low range of the approved label dose, marbofloxacin is active against most susceptible bacteria. Within the approved dose range, higher doses are needed for organisms with higher minimum inhibitory concentration (MIC) values. Doses published for European use are lower than US-approved doses, but there is no evidence that this has affected efficacy. For example, successful treatment of pyoderma in European studies has been accomplished with doses of 2.0 mg/kg once daily, but in the US, the lowest dose is 2.75 mg/kg once daily.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) break points for sensitive organisms in dogs and cats are  $\leq 1.0$  mcg/mL. If other fluoroquinolones are used to test susceptibility to marbofloxacin, results will be similar. However, marbofloxacin is slightly more active than other veterinary quinolones against *P. aeruginosa*.

## Formulations

- Marbofloxacin is available in 25-, 50-, 100-, and 200-mg tablets. Injectable marbofloxacin (Marbocyl 10%, 100 mg/mL) is approved in other countries but not in the US. A formulation in Europe is Forcyl, which is a 16% solution for IM or IV injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not compound with ingredients that may chelate with quinolones, such as iron or calcium.

## Small Animal Dosage

### Dogs

- 2.75-5.5 mg/kg once daily PO.

### Cats

- 2.75-5.5 mg/kg once daily PO.

## Large Animal Dosage

### Horses

- 2 mg/kg once daily IV or PO for treatment of susceptible gram-negative bacteria (IV formulation not available in the US). Because of low oral absorption in horses, the small animal dose of 2 mg/kg may not be sufficient for treating other bacteria that cause infections in horses, including gram-positive cocci. However, higher doses have not been tested.

### Calves

- 2 mg/kg, IV, SC, or IM in the neck once daily for 3-5 days, or 8-10 mg/kg once, IM.

### Pigs

- 2 mg/kg once per day IM (neck) for 3-5 days, or 8 mg/kg once.

## Regulatory Information

Marbofloxacin is prohibited from use in animals intended for food in the United States. There are no withdrawal times established because it should not be administered to animals that produce food. In the US, it is illegal to administer fluoroquinolones to food animals in an extralabel manner. Outside the U.S., withdrawal times have been established: 6 days withdrawal for meat at 2 mg/kg and 3 days at 8 mg/kg. Milk withdrawal is 36 hours at 2 mg/kg, and 72 hours at 8 mg/kg. Withdrawal time for pigs is 4 days.

## Maropitant Citrate

mar-op'i-tent

**Trade and other names:** Cerenia

**Functional classification:** Antiemetic

## Pharmacology and Mechanism of Action

Maropitant is an antiemetic from the same group as the human drug aprepitant (Emend). These drugs act as antiemetics by blocking the neurokinin-1 (NK1) receptor (also known as substance P). Neurokinin-1 is a neurotransmitter to stimulate vomiting from the emetic center. It has less affinity for other neurokinin receptors (NK2 and NK3). Although NK1 receptors are involved in other physiologic and

behavioral responses, at doses used to control vomiting, there were no adverse effects associated with blockade of other receptors. Maropitant can inhibit vomiting that is stimulated from both central and peripheral sources mediated by other neurotransmitters such as acetylcholine, histamine, dopamine, and serotonin. The NK1 receptor is also involved in transmission of pain (via substance P), and blockers of this receptor may have potential as adjunctive treatments for painful conditions.

In dogs, the peak concentration is achieved approximately 45 minutes after SQ administration. The half-life was 4-8 hours, depending on the dose. Dose-dependent pharmacokinetics occur, with the clearance decreasing and half-life increasing with doses above 2 mg/kg. Because of nonlinear pharmacokinetics, accumulation is possible with repeated dosing. Oral absorption is 24% at 2 mg/kg and 37% at 8 mg/kg in dogs. Pharmacokinetics are not affected by feeding. In cats, the clearance is much lower than in dogs, and the half-life is longer than in dogs, at 13-17 hours. In cats, it has nearly complete SQ absorption and 50% oral absorption.

### **Indications and Clinical Uses**

Maropitant is approved for use as an antiemetic in dogs to inhibit vomiting from both central and peripheral sources. It has been effective to inhibit vomiting from chemotherapy, gastrointestinal disease, toxins, renal disease, vestibular stimuli (motion sickness), and circulating stimuli via the chemoreceptor trigger zone (CRTZ). After SQ injection, it has a rapid onset with a peak concentration 45 minutes after injection and a duration of 24 hours. Maropitant also is approved for use in cats and has been used safely and effectively in cats to treat vomiting from a variety of sources, such as motion sickness and stimulation by emetogenic agents, with a duration of action of 24 hours.

Blockade of the NK1 receptor may have potential as an adjunctive treatment for some types of pain (e.g., visceral pain). Experimental studies have shown effects, but at this time, there are no clinical studies to demonstrate analgesic effects from maropitant.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Maropitant may cause slight pain or irritation from SQ injection. It has been recognized that the pain is caused by alteration of the formulation, which may occur when the injectable formulation is stored at room temperature. The cyclodextrin complex of maropitant is preserved at cold temperatures and is more stable and intact when the formulation is refrigerated. Therefore the adverse event associated with a painful injection can be reduced if injectable maropitant is stored in the refrigerator before use. Safety studies have been conducted with maropitant in both preclinical and clinical trials. In experimental dogs, it was safe at 3 times and 5 times the labeled dose. Adverse effects observed in trials included excess salivation and muscle tremors. In cats, it has been well tolerated at high doses (of a factor of 10 times) and was safe at 5 mg/kg for 15 consecutive days.

#### **Contraindications and Precautions**

There is accumulation after repeated doses and decreased clearance with higher doses. Therefore because of accumulation, the previous label states that it should not be administered for more than 5 consecutive days and one should allow a 2-day washout period before instituting another course of treatment. However, follow-up studies and a new revised label indicate that it may be safely administered to dogs at 8 mg/kg for 14 consecutive days and the label has been extended to indicate that it may be administered until the condition has been resolved in dogs 7 months of age or older. When treating protracted vomiting, veterinarians should attempt to identify any underlying disease whenever possible.

instead of relying on maropitant to control the clinical signs. Maropitant effects and pharmacokinetics are not affected by kidney disease.

### Drug Interactions

Single doses have been administered in an IV line, but precipitation may be observed if mixed with alkalinizing solutions. Maropitant is an NK<sub>1</sub> inhibitor. Other neurokinin receptors are affected to a lesser degree. Because of the unique mechanism of action, drug interactions have not been identified. Maropitant has been used safely with other drugs, including anesthetics and anticancer agents. Maropitant is highly protein bound, but it is not known if there are protein-binding interactions with other drugs.

### Instructions for Use

Clinical trials in dogs have outlined the appropriate protocols for use of maropitant. It has been effective for a wide range of causes of vomiting in dogs. In dogs, it was more effective to prevent opiate-induced vomiting if administered at least 30 minutes prior to the opiate administration, but to prevent nausea, 60 minutes prior is suggested. It is also approved in cats for prevention of vomiting. It has been effective for a variety of causes of vomiting, including motion sickness and stimulation from emetogenic agents. The effective dose in cats is 1 mg/kg, regardless of cause.

### Patient Monitoring and Laboratory Tests

Monitor for clinical signs and disease that may be a cause for the vomiting. Other specific monitoring and tests are not needed to use maropitant safely.

### Formulations

- Maropitant is available in 16-, 24-, 60-, or 160-mg tablets and a 10-mg/mL injectable solution.

### Stability and Storage

Store in a tightly sealed container, protected from light. The injectable formulation can be stored at room temperature and in the refrigerator, but as noted earlier, pain from injection can be reduced if the formulation is stored in the refrigerator. Discard vial after 28 days of first use.

### Small Animal Dosage

#### Dogs

- 1 mg/kg SQ, or 2 mg/kg PO, once daily, for up to 5 days in dogs 2-7 months of age, and until the problem is resolved for dogs older than 7 months.
- Motion sickness: 8 mg/kg PO once daily for up to 2 consecutive days.
- To prevent opioid-induced vomiting: 2-4 mg/kg PO prior to anesthetic procedure.

#### Cats

- 1 mg/kg once daily IV, SQ, or PO (same dose for all causes of vomiting, including motion sickness).
- To decrease vomiting and nausea from kidney disease: 4 mg per cat per day PO.

### Large Animal Dosage

- No large animal doses have been identified.

### Regulatory Information

No regulatory information is available for food animals. There are no withdrawal times established, and it is not recommended to be administered to animals that produce food.

## Masitinib Mesylate

**Trade and other names:** Kinavet-CA1 (US), Masivet (Europe)

**Functional classification:** Anticancer agent.

### Pharmacology and Mechanism of Action

Masitinib is an antitumor agent used primarily for mast cell tumors, but may have effects on other tumors. Masitinib is a tyrosine kinase inhibitor (TKI) that targets the c-Kit pathway. It is more specific for inhibiting the stem cell factor that regulates mast cell tumor proliferation. It exerts direct antiproliferative actions on mast cells through disruption of the stem cell factor, mast cell c-Kit pathway. It is also effective for canine atopic dermatitis in limited studies. There is also evidence that masitinib may revert the multi-drug resistance (MDR) to a normal state in drug-resistant cancer cells. This mechanism reduced the *in vitro* doxorubicin drug resistance in canine cancer cells, but has not been confirmed in clinical studies.

For canine atopic dermatitis, it is used at a dose of 12.5 mg/kg per day. It has moderate effectiveness. The effectiveness implies that mast cells may be involved in the pathogenesis of atopic dermatitis.

### Indications and Clinical Uses

Masitinib is used to treat mast cell tumors in dogs. It is indicated for the treatment of nonresectable grade II or III cutaneous mast cell tumors in dogs.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects in dogs may include gastrointestinal disturbance and reversible protein loss. Cats are particularly prone to vomiting and diarrhea (most common), as well as proteinuria and neutropenia.

#### Contraindications and Precautions

No contraindications reported.

#### Drug Interactions

No drug interactions reported.

### Instructions for Use

Results of clinical trials using masitinib have primarily involved mast cell tumors. Medical oncologists are investigating other uses for this medication.

### Patient Monitoring and Laboratory Tests

Because of risk of protein loss, monitor serum protein and urine protein periodically during treatment.

### Formulations

- Masitinib is available in 50 and 150 mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, at room temperature, and in a cool place. The tablets are coated and should not be broken or crushed.

### Small Animal Dosage

- Dogs: Mast cell tumors: 12.5 mg/kg PO once per day.  
Dogs: Atopic dermatitis, 12.5 mg/kg per day, PO.

- Cats: It was tolerated in most cats at a dose of 50 mg per cat every day, or every other day for 4 weeks, but clinical use has not been established.

### Large Animal Dosage

- No large animal doses have been reported.

### Regulatory Information

Do not administer to food-producing animals.

## MCT Oil

**Trade and other names:** Medium-chain triglycerides (MCT) oil

**Functional classification:** Nutritional supplement

### Pharmacology and Mechanism of Action

MCT oil supplements triglycerides in animals.

### Indications and Clinical Uses

MCT oil is used to treat lymphangiectasia and as a component of enteral feeding formulas.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects not reported in veterinary medicine. It may cause diarrhea in some patients.

#### Contraindications and Precautions

No contraindications reported.

#### Drug Interactions

No drug interactions reported.

### Instructions for Use

Results of clinical trials using MCT oil have not been reported. Many enteral feeding formulas contain MCT oil (many polymeric formulations).

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- MCT oil is available as an oral liquid.

### Stability and Storage

Store in a tightly sealed container, protected from light, at room temperature, and in a cool place. Do not store in a plastic container. It may be mixed with fruit juices or food products prior to administration.

### Small Animal Dosage

- 1-2 mL/kg daily in food.

### Large Animal Dosage

- No large animal doses have been reported.

### Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.



## Mebendazole

meh-ben'dah-zole

**Trade and other names:** Telmintic, Telmin, Vermox (human preparation), and generic brands

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Benzimidazole antiparasitic drug. Like other benzimidazoles, mebendazole produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in the parasite, eventually resulting in death. However, there is no effect on glucose metabolism in mammals.

### Indications and Clinical Uses

Mebendazole is used in horses for treatment of infections caused by large roundworms (*Parascaris equorum*), large strongyles (*Strongylus edentatus*, *S. equinus*, and *S. vulgaris*), small strongyles, and mature and immature (fourth larval stage pinworms [*Oxyuris equi*]). In dogs, it has been used for treatment of infections of roundworms (*Toxocara canis*), hookworms (*Ancylostoma caninum* and *Uncinaria stenocephala*), whipworms (*Trichuris vulpis*), and tapeworms (*Taenia pisiformis*).

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are rare. Mebendazole causes occasional vomiting and diarrhea in dogs. Some reports suggest idiosyncratic hepatic reactions in dogs.

#### Contraindications and Precautions

No contraindications have been reported.

#### Drug Interactions

No drug interactions have been reported for animals.

### Instructions for Use

The powder for horses may be sprinkled directly on the horse's grain or dissolved in 1 L of water and administered via stomach tube. For dogs, it may be added directly to food.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Mebendazole is available in 40- or 166.7-mg/g powder, 200-mg/g equine paste, 33.3-mg/mL solution, and 100-mg chewable tablets (human preparation). Equine formulations contain either 83.3 mg mebendazole plus 375 mg trichlorfon or 100 mg mebendazole plus 454 mg trichlorfon in each gram of powder. The combination (Telmin) is a 33-mg/mL liquid suspension.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 22 mg/kg (mixed with food) q24h for 3 days. May be repeated in 3 weeks.

## Large Animal Dosage

### Horses

- 8.8 mg/kg PO.

## Regulatory Information

Do not administer to horses intended for food.

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

## Meclizine

mek'lih-zeen

**Trade and other names:** Antivert, Bonine, Meclozine (British name), and generic brands

**Functional classification:** Antiemetic, and antihistamine

M

## Pharmacology and Mechanism of Action

Antiemetic. Antihistamine. Like other antihistamines, it blocks the effect of histamine on the H<sub>1</sub> receptor. However, it also has central anticholinergic actions, which may be responsible for the central-acting antiemetic properties.

## Indications and Clinical Uses

Meclizine is used to treat vomiting. It may suppress the chemoreceptor trigger-zone (CRTZ). It also is used for treatment of motion sickness. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Other drugs with proven efficacy (e.g., maropitant) are often used instead of meclizine for vomiting.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals. Anticholinergic (atropine-like) effects may cause side effects.

### Contraindications and Precautions

Use cautiously in animals with gastrointestinal obstruction or glaucoma.

### Drug Interactions

No drug interactions have been reported for animals.

## Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals is based on experience in people or anecdotal experiences in animals.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## **Formulations**

- Meclizine is available in 12.5-, 25-, and 50-mg tablets.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## **Small Animal Dosage**

### **Dogs**

- 25 mg per dog q24h PO (for motion sickness, administer 1 hour prior to traveling).

### **Cats**

- 12.5 mg per cat q24h PO (for motion sickness, administer 1 hour prior to traveling).

## **Large Animal Dosage**

- No large animal doses have been reported.

## **Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## **Meclofenamate Sodium, Meclofenamic Acid**

mek'loe-fen'am-ate soe-dee'um, mek'loe-fen-am'ik ass'id

**Trade and other names:** Arquel and Meclofen

**Functional classification:** Nonsteroidal anti-inflammatory drug (NSAID)

## **Pharmacology and Mechanism of Action**

Meclofenamate is also known as meclofenamic acid and is related to tolfenamic acid, which is approved in some countries for animals. Meclofenamate and other nonsteroidal anti-inflammatory drugs (NSAIDs) have produced analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclooxygenase (COX) enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy gastrointestinal tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, there may be some crossover of these properties. Meclofenamic acid is a balanced COX-1/COX-2 inhibitor.

## **Indications and Clinical Uses**

Meclofenamate is used in animals for treatment of pain and inflammation. The most common use has been musculoskeletal inflammation. Use in animals has diminished because of decreased availability and increased popularity of other drugs.

## **Precautionary Information**

### **Adverse Reactions and Side Effects**

Adverse effects have not been reported in animals, but adverse effects common to other NSAIDs are possible. These side effects are generally gastrointestinal in nature (e.g., gastritis, gastric ulcers).

### Contraindications and Precautions

Do not administer to animals prone to gastrointestinal ulcers. Do not administer with other ulcerogenic drugs such as corticosteroids. The original approved labeling for animals suggests that duration is limited to 5-7 days.

### Drug Interactions

Like other NSAIDs, ulcerogenic effects are potentiated when administered with corticosteroids. Meclofenamic acid, like other NSAIDs, may interfere with the action of diuretics, such as furosemide, and angiotensin-converting enzyme (ACE) inhibitors.

### Instructions for Use

Most of the experience with meclofenamate has been with horses. Commercial formulations are no longer marketed for animals in the United States. Administer with food.

### Patient Monitoring and Laboratory Tests

Monitor for signs of gastrointestinal ulceration during use.

### Formulations

- Meclofenamate is available in 50- and 100-mg capsules (rarely available commercially any longer), 10- and 20-mg tablets (formulation for dogs), and granules for horses (5% meclofenamic acid).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 1.1 mg/kg/day for up to 5 days PO.

### Large Animal Dosage

#### Horses

- 2.2 mg/kg q24h PO.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). Racing Commissioners International (RCI) Classification: 4

## Medetomidine Hydrochloride

meh-deh-toe'mih-deen hye-droe-klor'ide

**Trade and other names:** Domitor

**Functional classification:** Analgesic,  $\alpha_2$  agonist

**Note:** The marketing of medetomidine has been discontinued in most countries and this product is no longer available. It has been replaced by dexmedetomidine (Dexdomitor), which consists of the active D-isomer.

### Pharmacology and Mechanism of Action

$\alpha_2$ -adrenergic agonist.  $\alpha_2$  agonists decrease release of neurotransmitters from the neuron. Medetomidine is a racemic mixture containing 50% dexmedetomidine and 50% levomedetomidine. Dexmedetomidine is the active enantiomer of the

mixture (D-isomer); therefore (on a mg/mg basis) dexmedetomidine is twice the potency of medetomidine but with the same pharmacological activity and equivalent analgesic and sedative effects. The proposed mechanism whereby the  $\alpha_2$  agonists decrease transmission is via binding to presynaptic  $\alpha_2$  receptors (negative feedback receptors). The result is decreased sympathetic outflow, analgesia, sedation, and anesthesia. Other drugs in this class include xylazine, detomidine, and clonidine. Receptor-binding studies indicate that  $\alpha_2/\alpha_1$ -adrenergic receptor selectivity for medetomidine was more than 1000-fold greater than xylazine.

### **Indications and Clinical Uses**

Because of potency and availability, dexmedetomidine has replaced medetomidine for most indications in small animals. Medetomidine, like other  $\alpha_2$  agonists, is used as a sedative, anesthetic adjunct, and analgesic. Duration of effect is 0.5-1.5 hours at the low dose and up to 3 hours for the high dose. Compared to xylazine, medetomidine has produced better sedation and analgesia than xylazine in dogs. Many anesthesiologists have recommended combinations of medetomidine and ketamine, medetomidine and butorphanol, or medetomidine and hydromorphone in dogs for sedation and short-term procedures. Medetomidine combined with an opiate (butorphanol or hydromorphone) has produced a longer duration of sedation and more desirable degree of sedation than medetomidine used alone. It has been used to sedate animals for intradermal skin testing without affecting results.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

In small animals, vomiting is the most common acute effect.  $\alpha_2$  agonists decrease sympathetic output. Cardiovascular depression may occur. Constant-rate infusion of 1.5 mcg/kg/hr has caused decreased heart rate and sinus arrhythmia in dogs. Doses as low as 1 mcg/kg IV can reduce cardiac output to less than 40% of resting value. Medetomidine will cause initial bradycardia and hypertension, but bradycardia usually does not require intervention with anticholinergic drugs (e.g., atropine). If adverse reactions are observed, reverse with atipamezole. If atipamezole is not available, yohimbine also can reverse medetomidine.

#### **Contraindications and Precautions**

Use cautiously in animals with heart disease. Use may be contraindicated in older animals with preexisting cardiac disease. Xylazine causes problems in pregnant animals, and this also should be considered for other  $\alpha_2$  agonists. Use cautiously in animals that are pregnant because it may induce labor. In addition, it may decrease oxygen delivery to the fetus in late gestation.

#### **Drug Interactions**

Do not use with other drugs that may cause cardiac depression. Do not mix in a vial or syringe with other anesthetics, except as listed under the dosing section. Reverse with atipamezole at a dose of 25-300 mcg/kg IM. Use with opioid analgesic drugs will greatly enhance the CNS depression, so consider lowering doses if administered with opioids.

### **Instructions for Use**

Medetomidine, dexmedetomidine, and detomidine are more specific for the  $\alpha_2$  receptor than xylazine. Dexmedetomidine has twice the potency of medetomidine. Therefore these drugs should not be used interchangeably without consulting the dose recommendations. The  $\alpha_2$  agonists may be used for sedation, analgesia, and minor surgical procedures. Many veterinarians use doses that are much less than the doses listed on the label. For example, lower doses are sometimes used for short-term sedation and

analgesia, particularly when combined with other drugs such as opiates. Reverse with atipamezole at a dose of 25-300 mcg/kg (equal to volume of medetomidine used) IM.

### Patient Monitoring and Laboratory Tests

Monitor vital signs during anesthesia. Monitor heart rate, blood pressure, and ECG if possible during anesthesia.

### Formulations

- Medetomidine is available in a 1.0-mg/mL injection. The commercial form has been discontinued in many countries and replaced by dexmedetomidine.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 750 mcg/m<sup>2</sup> IV or 1000 mcg/m<sup>2</sup> IM. The IV dose is equivalent to 18-71 mcg/kg IV.
- Lower doses are often used for short-term sedation and analgesia of 5-15 mcg/kg (0.005-0.015 mg/kg) IV, IM, or SQ. These doses may be increased up to 60 mcg/kg when severe pain is involved. 20 mcg/kg has been used in combination with butorphanol (0.2 mg/kg), hydromorphone (0.1 mg/kg), or ketamine for short-term procedures.
- CRI: Loading dose of 1 mcg/kg IV, followed by 0.0015 mg/kg/hr (1.5 mcg/kg/hr). Constant-rate infusion may produce adverse cardiovascular effects and should be monitored closely.

#### Cats

- 750 mcg/m<sup>2</sup> IV or 1000 mcg/m<sup>2</sup> IM. The IV dose is equivalent to 18-71 mcg/kg IV. Doses in the lower range are used for short-term sedation and analgesia (e.g., 10-20 mcg/kg), but higher doses (up to 80 mcg/kg) have been used for more severe pain. Medetomidine may be administered IM or IV.
- Combination with ketamine: 5 mg/kg ketamine + 5 mcg/kg medetomidine mixed in one syringe and administered IM.

### Large Animal Dosage

#### Lambs

- 30 mcg/kg (0.03 mg/kg) IV.

#### Horses

- 10 mcg/kg IM as a sedative prior to induction for anesthesia. Some horses may need an additional dose of 4 mcg/kg IV. In horses, guaifenesin (5% solution) and ketamine (2.2 mg/kg) have been used in combination.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 3

## Medroxyprogesterone Acetate

meh-droks'ee-proe-jess'teh-rone ass'ih-tate

**Trade and other names:** Depo-Provera (injection), Provera (tablets), and Cycrin (tablets)

**Functional classification:** Hormone

## **Pharmacology and Mechanism of Action**

Progestin hormone. Medroxyprogesterone is a derivative of acetoxyprogesterone. Medroxyprogesterone acetate replaces progesterone in the body and will mimic progesterone's hormone effects. In the Depo-Provera formulation, a single injection can produce long-acting effects.

## **Indications and Clinical Uses**

Medroxyprogesterone acetate is used to replace progesterone in animals. Most often it is used as progesterone hormone treatment to control the estrus cycle. It also is used for management of some behavioral and dermatologic disorders (such as urine spraying in cats and alopecia). However, its use for behavioral therapy in animals is discouraged because of high relapse rates and incidence of hormone-related adverse effects. In horses, it has been used to prevent estrus.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects include polyphagia, polydipsia, adrenal suppression (cats), increased risk of diabetes mellitus, pyometra, diarrhea, and increased risk of neoplasia. In cats, a single injection of medroxyprogesterone acetate has produced feline mammary fibroepithelial hyperplasia.

#### **Contraindications and Precautions**

Do not use in animals at a high risk for diabetes. In humans, it increases the risk of thromboembolic problems. Do not use in pregnant animals.

#### **Drug Interactions**

No drug interactions are reported. However, clearance of medroxyprogesterone is increased with drugs known to induce hepatic P450 enzymes (see Appendix H).

## **Instructions for Use**

Intervals of administration vary with condition. Intervals may range from once a week to once a month.

Clinical studies in animals have studied primarily the reproductive use and effects on behavioral use. Medroxyprogesterone acetate may have fewer side effects than megestrol acetate.

## **Patient Monitoring and Laboratory Tests**

It may increase concentrations of serum cholesterol and some liver enzymes.

## **Formulations**

- Medroxyprogesterone is available in 150- and 400-mg/mL suspension injection and 2.5-, 5-, and 10-mg tablets.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## **Small Animal Dosage**

### **Dogs and Cats**

- 1.1-2.2 mg/kg every 7 days IM.
- Behavior problems: 5 mg per dog once daily as needed.
- Prostatic disease (dogs): 3-5 mg/kg IM or SQ every 3-4 weeks.

## Large Animal Dosage

### Horses

- Prevent estrus: 250-500 mg/horse IM.

## Regulatory Information

There are no withdrawal times established because this drug should not be administered to animals that produce food.

## Megestrol Acetate

meh-jess'trole ass'ih-tate

**Trade and other names:** Ovaban and Megace

**Functional classification:** Hormone

## Pharmacology and Mechanism of Action

Progestin hormone. Megestrol acetate mimics the effects of progesterone in animals.

## Indications and Clinical Uses

Megestrol acetate is used in animals as a progesterone hormone treatment to control the estrus cycle, for example to postpone the estrus cycle. It is also used in female dogs for the alleviation of false pregnancy. It also has been used for management of some behavioral and dermatologic disorders (such as urine spraying in cats and alopecia). However, its use for behavioral therapy in animals is discouraged because of high relapse rates and incidence of hormone-related adverse effects.

In horses, it has been used to prevent estrus, but efficacy for this indication has not been good at doses of 10-20 mg/day/horse.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects include polyphagia, polydipsia, adrenal suppression (cats), increased risk of diabetes, pyometra, diarrhea, and increased risk of neoplasia.

### Contraindications and Precautions

Do not use in diabetic animals or animals that may be at risk for developing diabetes. Do not use in pregnant animals. Do not administer for more than two consecutive treatments. Do not use prior to or during first estrus cycle. Do not use in the presence of a disease of the reproductive system or with mammary tumors. Should estrus occur within 30 days after cessation of treatment, mating should be prevented.

### Drug Interactions

No drug interactions are reported. However, clearance of medroxyprogesterone is increased with drugs known to induce hepatic P450 enzymes (see Appendix H).

## Instructions for Use

Clinical studies in animals have studied primarily the reproductive use and effects on behavioral use. Medroxyprogesterone acetate may have fewer side effects than megestrol acetate. When used for proestrus treatment, administer 2.2 mg/kg for 8 days administered orally. For anestrus treatment, administer 0.55 mg/kg per day for 32 days. Tablets can be administered intact, or crushed and mixed with food. Once therapy is started, the animal should be confined for 3 to 8 days or until cessation of bleeding, since dogs in proestrus accept a male.



**Patient Monitoring and Laboratory Tests**

Because of risk of diabetes mellitus, monitor glucose concentrations during treatment periodically. Examination of vaginal smears is recommended to confirm detection of proestrus.

**Formulations**

- Megestrol acetate is available in 5- and 20-mg tablets (veterinary preparation) and 20- and 40-mg tablets (human preparation).

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- Proestrus: 2 mg/kg q24h PO for 8 days (early proestrus).
- Anestrus: 0.5 mg/kg q24h PO for 32 days.
- Treatment of behavior problems: 2-4 mg/kg q24h for 8 days (reduce dose for maintenance).

**Cats**

- Dermatologic therapy or urine spraying: 2.5-5 mg/cat q24h PO for 1 week, then reduce to 5 mg once or twice a week per cat.
- Suppress estrus: 5 mg/cat/day for 3 days, then 2.5-5 mg once a week for 10 weeks.

**Large Animal Dosage****Horses**

- Suppress estrus: 0.5 mg/kg q24h PO.

**Regulatory Information**

There are no withdrawal times established because this drug should not be administered to animals that produce food.

**Melarsomine Dihydrochloride**

mel-ar'soe-meen

**Trade and other names:** Immiticide

**Functional classification:** Antiparasitic

**Pharmacology and Mechanism of Action**

Organic arsenical compound. Arsenicals alter glucose uptake and metabolism to eliminate heartworms. Melarsomine has replaced older arsenicals such as thiacetarsamide (Caparsolate).

**Indications and Clinical Uses**

Melarsomine is used for heartworm adulticide therapy. See “[Instructions for Use](#)” for proper administration. Melarsomine is highly effective for eliminating heartworms in dogs. Efficacy in cats is only 36%. Usually, cats are not treated because it is a self-limiting disease and only supportive treatment is administered (corticosteroids, bronchodilators, and antiemetics).

**Precautionary Information****Adverse Reactions and Side Effects**

Melarsomine administration may lead to pulmonary thromboembolism 7-20 days after therapy, anorexia (13% incidence), injection-site reaction (32% incidence of

myositis), or lethargy or depression (15% incidence). It causes elevations of hepatic enzymes. High doses (three times the dose) can cause pulmonary inflammation and death. If high doses are administered, dimercaprol (3 mg/kg IM) may be used as antidote. To prevent adverse reactions of adulticide therapy, many veterinarians administer prednisolone or prednisone at a dose of 0.5 mg/kg q12h for the first week and 0.5 mg/kg q24h for the second week, followed by 0.5 mg/kg every other day for 1-2 weeks. There is also evidence that doxycycline (10 or 20 mg/kg per day PO) may decrease pulmonary reactions to melarsomine therapy.

### Contraindications and Precautions

Use cautiously in animals with high heartworm burden. Specifically, melarsomine is contraindicated in dogs with Class 4 (very severe) heartworm disease.

### Drug Interactions

No drug interactions are reported. Administration of prednisolone does not affect efficacy of melarsomine.

## Instructions for Use

Dose regimens are based on severity of heartworm disease. Follow product insert carefully for instructions on proper administration. Also evaluate patient to determine class of heartworm disease (Class 1-4) before initiating treatment. Class 1 and 2 are least severe. Class 3 is severe, and Class 4 is most severe and should not be treated with adulticide before surgery. In animals with severe burdens, and even including Class 1 and 2 patients, some cardiologists recommend using a three-dose protocol. The three-dose protocol includes a single IM injection of 2.5 mg/kg to decrease the initial worm burden; then administer two additional doses, 24 hours apart, at least one month later (2 or 3 months is acceptable). Alternatively, there may be benefits for administering a preventive dose of a macrocyclic lactone (e.g., ivermectin or related drug) with doxycycline for 30 days, followed by the first injection of melarsomine at 60 days and two more injections of melarsomine at 90 days. Avoid human exposure by either washing hands after handling or wearing gloves. There should be strict exercise restriction in dogs during adulticide treatment. More details on the protocol for administration can be found at the American Heartworm Society's website (<http://www.heartwormsociety.org/>).

## Patient Monitoring and Laboratory Tests

Monitor heartworm status and microfilaria after treatment. Monitor treated patients carefully for signs of pulmonary thromboembolism.

## Formulations

- Melarsomine is available in a 25-mg/mL injection.

## Stability and Storage

After reconstitution, solution retains potency for 24 hours. Do not freeze solutions after they are prepared.

## Small Animal Dosage

### Dogs

- Administer via deep IM injection.
- Class 1-2: 2.5 mg/kg/day for 2 consecutive days. See “Instructions for Use” section for more alternative protocols for these patients.
- Class 3: 2.5 mg/kg once, then in 1 month two additional doses 24 hours apart.

### Cats

- Not recommended.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

There are no withdrawal times established because this drug should not be administered to animals that produce food.

## Meloxicam

mel-oks'ih-kam

**Trade and other names:** Metacam, OroCAM, Loxicom (veterinary preparations), Mobic (human preparation), Metacam suspension (equine preparation, Europe), and Mobicox (human formulation in Canada)

**Functional classification:** Anti-inflammatory

## Pharmacology and Mechanism of Action

Meloxicam is a nonsteroidal anti-inflammatory drug (NSAID). Like other NSAIDs meloxicam has analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the COX enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy gastrointestinal tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects, and COX-2 activity is important for some biological effects. Meloxicam is relatively COX-1 sparing compared to older NSAIDs, but it is not known if the specificity for COX-1 or COX-2 is related to efficacy or safety. Meloxicam has a half-life of 23-24 hours in dogs, 30-40 hours in calves, and 8.5 (range 5-14.5) in horses. In cats, it had a half-life of 15 hours in experimental cats, but in a larger population pharmacokinetic study, the half-life was 26 hours, with volume of distribution of 0.24 L/kg. Meloxicam is highly protein bound. Oral absorption is almost complete in dogs when administered with food. Absorption is 85%-98% in horses and is not affected significantly by feeding. Oral absorption was 100% in ruminant calves, with a half-life of 20-43 hours, and 79% and 72% in goats and sheep, respectively.

## Indications and Clinical Uses

Meloxicam is used to decrease pain, inflammation, and fever. It has been used for the acute and chronic treatment of pain and inflammation in dogs and cats. One of the most common uses is osteoarthritis, but it has also been used for pain associated with surgery. Both acute and long-term safety and efficacy have been established for dogs. In studies performed in dogs, higher doses (up to 0.5 mg/kg) were more effective than lower doses, but also were associated with a higher incidence of gastrointestinal adverse effects. Use in cats is limited to either short-term use or long-term use at low doses. In cats, meloxicam has comparable, and even superior, effectiveness compared to butorphanol for treating pain associated with surgery. Acute response to treating fever in cats also has been demonstrated. In pigs, meloxicam is effective for mastitis-metritis-agalactia (MMA) syndrome. In horses, meloxicam is effective for treating pain and inflammation associated with surgery. A dose of 0.6 mg/kg per day to horses for long periods (6 weeks) was well tolerated and produces plasma drug concentrations in the therapeutic range. In European countries, it is registered for use in horses, pigs, and cattle. In these countries, the approved use is adjunctive therapy of acute respiratory disease, diarrhea, and acute mastitis. It has also been effective to decrease discomfort associated

with dehorning procedures in cattle. Meloxicam also is used extralabel in many exotic and zoo animals, including reptiles and birds, for treatment of pain and inflammation.

## Precautionary Information

### Adverse Reactions and Side Effects

Major adverse effects are gastrointestinal, including vomiting, diarrhea, and ulceration. Because meloxicam appears to be relatively COX-1 sparing, adverse effects are expected to be less than other NSAIDs that are not as selective, but this has not been demonstrated on controlled clinical trials. Kidney injury, especially in dehydrated animals or animals with preexisting renal disease, has been shown for some NSAIDs. Kidney injury has been reported in dogs from doses of 0.3-0.5 mg/kg, and higher. Gastrointestinal ulceration has been observed when dogs were administered doses slightly higher than registered doses. In cats at high doses (five times the dose), vomiting and other gastrointestinal problems were reported. With repeated doses (9 days) of 0.3 mg/kg/day to cats, inflamed gastrointestinal mucosa and ulceration were observed. At 0.05 mg/kg there were not changes on platelet aggregation in cats. Kidney injury has been observed in cats, particularly when high doses were administered repeatedly or when administered at lower doses to dehydrated cats. However, there is no evidence that well-hydrated cats with kidney disease are more dependent on renal prostaglandins to maintain kidney perfusion; therefore meloxicam may be administered to these cats at low doses if hydration is maintained. At the recommended dose of 0.6 mg/kg to horses, it has been well tolerated but at high doses to horses (3-5 times the recommended dose), there was decreased protein, gastrointestinal injury, and kidney injury.

### Contraindications and Precautions

Dogs and cats with preexisting gastrointestinal problems or renal problems may be at a greater risk of adverse effects from NSAIDs. However, at a dose of 0.02 mg/kg per day, long-term use in cats did not cause progression of renal disease in cats with preexisting renal disease. Safety in pregnant animals is not known, but adverse effects have not been reported. The manufacturer does not recommend a second dose of meloxicam injection to cats. The oral meloxicam solution of meloxicam contains xylitol. Xylitol is an artificial sweetener that can be toxic to dogs and can produce hypoglycemia and liver injury with high doses exceeding 0.1 g/kg. With approved doses of meloxicam oral solution, the toxic level of xylitol is not likely to be exceeded, but one should be cautious about adding other drugs that also contain xylitol.

### Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the gastrointestinal adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and ACE inhibitors.

## Instructions for Use

Liquid medication may be added to food for dosing. When using veterinary liquid formulation, the dropper bottle for the 1.5 mg/mL suspension is designed to deliver 0.05 mg per drop or one drop per pound body weight (two drops per kg body weight). Observe manufacturer's instructions when using dosing syringe supplied with product. Some veterinarians have used the human generic tablets for administration to horses and dogs. The human formulation has been shown to be absorbed to the same extent as the veterinary formulations. However, caution is advised when administering the oral human tablets to dogs. The tablet size (7.5 mg) is much larger than the highest dose that should be administered to dogs.

Administration to cats in the US is only approved as a single dose of 0.3 mg/kg. However, long-term use at 0.05 mg/kg q24h oral has been approved for cats in

other countries for prolonged use, and low doses 0.01-0.03 mg/kg q24h have been administered safely to older cats with kidney disease.

### **Patient Monitoring and Laboratory Tests**

Monitor gastrointestinal signs for evidence of diarrhea, gastrointestinal bleeding, or ulcers. Because of risk of renal injury, monitor renal parameters (water consumption, blood urea nitrogen [BUN], creatinine, and urine-specific gravity) periodically during treatment.

### **Formulations**

- Meloxicam is available in 0.5-mg/mL (0.02 mg per drop) oral suspension, 1.5-mg/mL (0.05 mg per drop) oral suspension, 0.5% (5-mg/mL) injection, and 7.5- and 15-mg tablets (human preparation). An oral transmucosal is available as a spray using the Promist technology. The spray is available in three sizes: 0.25 mg, 0.5 mg, and 1.075 mg per spray.
- In Europe, 1.0 and 2.5 mg/kg tablets are available for dogs and a 15-mg/mL oral suspension and 50 mg per gram oral paste is available for horses. In Europe a 20 mg/mL injectable solution is available for large animals.

### **Stability and Storage**

Meloxicam has been compounded with water, 1% methylcellulose gel, and simple syrup or a suspending and flavoring vehicle in a ratio of 1:1 at concentrations of 0.25, 0.5, and 1.0 mg/mL. These formulations were stable for 28 days at room temperature or under refrigeration.

### **Small Animal Dosage**

#### **Dogs**

- 0.2 mg/kg initial loading dose PO, SQ, or IV, and then 0.1 mg/kg q24h thereafter PO, SQ, or IV.
- Oral transmucosal spray (bioequivalent to oral suspension): 0.1 mg/kg sprayed in dog's mouth once per day.

#### **Cats**

- 0.05 mg/kg q24h PO, with reduction in dose if chronic treatment is pursued. Long-term treatment may be reduced to 0.03 mg/kg q24h, or 0.05 mg/kg q48h, to 0.05 mg/kg q72h, PO.
- Single doses of 0.15 mg/kg SQ may be administered for acute conditions. (There is Food and Drug Administration [FDA] approval in the US for single doses up to 0.3 mg/kg SQ.)

### **Large Animal Dosage**

#### **Pigs**

- 0.4 mg/kg IM, which may be repeated in 24 hours.

#### **Cattle**

- 0.5 mg/kg q24h IV, IM, or SQ.

#### **Sheep and Small Ruminants**

- 1 mg/kg, single dose, IV, IM, SQ, or PO.

#### **Horses**

- 0.6 mg/kg q24h IV or PO. In foals less than 7 weeks of age, the frequency may be increased to 0.6 mg/kg q12h because of more rapid clearance.

### **Regulatory Information**

Recommended withdrawal time for racing horses is 3 days for urine testing. Recommended cattle withdrawal time: 8-20 days for slaughter (depending on the study and

the country). Generally 20 days for slaughter is used. Withdrawal time for milk is 3.5-6 days, depending on the study and country of approval.

RCI Classification: 3

## Melphalan

mel'fah-lan

**Trade and other names:** Alkeran

**Functional classification:** Anticancer agent

### Pharmacology and Mechanism of Action

Anticancer agent. Melphalan is an alkylating agent, similar in action to cyclophosphamide. It alkylates base pairs in DNA and produces a cytotoxic effect.

### Indications and Clinical Uses

Melphalan is not used as an anticancer agent as frequently as other alkylating agents. In animals, it is used to treat multiple myeloma and certain carcinomas.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are related to its action as an anticancer agent. Melphalan causes myelosuppression.

#### Contraindications and Precautions

Do not use in animals with bone marrow suppression.

#### Drug Interactions

No drug interactions are reported. It has been used with other anticancer drug protocols.

### Instructions for Use

Consult specific anticancer drug protocols for more dosing information.

### Patient Monitoring and Laboratory Tests

Monitor complete blood count (CBC) for evidence of bone marrow toxicity.

### Formulations Available

- Melphalan is available in 2-mg tablets and 50-mg vials for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is insoluble in water but is soluble in ethanol. After reconstitution, decomposition occurs rapidly and may precipitate. Use within 1 hour of reconstitution. When prepared in a compounded formulation for oral use, it was unstable with rapid decomposition (80% loss in 24 hours).

### Small Animal Dosage

#### Dogs

- 1.5 mg/m<sup>2</sup> (or 0.1-0.2 mg/kg) q24h PO for 7-10 days (repeat every 3 weeks) or administer 7 mg/m<sup>2</sup> q24h, PO, for 5 days. Repeat this cycle every 21 days.
- Injectable forms have not been used in animals, but in humans, 16 mg/m<sup>2</sup> IV over 15-20 minutes has been used at 2-week intervals for multiple myeloma.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

**Meperidine Hydrochloride**

meh-pare'ih-deen hye-droe-klor'ide

**Trade and other names:** Demerol, Pethidine (European name)

**Functional classification:** Analgesic, opioid

**Pharmacology and Mechanism of Action**

Meperidine is a synthetic opioid agonist with activity primarily at the mu-opiate receptor. It is called pethidine in Europe. It is similar in action to morphine, except with approximately one seventh of the potency. An IM injection of 75 mg or an oral dose of 300 mg of meperidine has similar potency to 10 mg of morphine. Clearance is rapid in small animals after meperidine administration, and duration of effect is short.

**Indications and Clinical Uses**

Meperidine has been used for short-term sedative effects, often used with other sedatives and/or anesthetics. For analgesic use, it is short acting, usually less than 2 hours and often much shorter. Therefore its use for treating pain has not been popular and has been replaced by other opiate drugs. Meperidine may produce fewer gastrointestinal motility problems compared to other opioids. The use of meperidine in human medicine has declined because toxic effects have been observed from accumulation of metabolites.

**Precautionary Information****Adverse Reactions and Side Effects**

Like all opiates, some side effects are predictable and unavoidable. Side effects include sedation, urine retention, constipation, and bradycardia. Respiratory depression occurs with high doses. Tolerance and dependence occur with chronic administration. Repeated doses in humans may cause toxicity from accumulation of metabolite. One of the metabolites, normeperidine, accumulates with repeated administration because it has a half-life much longer than meperidine. The accumulation of the metabolite causes excitatory effects that may be related to serotonergic properties. Similar reactions have not been reported from clinical use in animals (see “[Drug Interactions](#)” section for other precautions).

**Contraindications and Precautions**

Meperidine is a Schedule II controlled substance. Cats are more sensitive to excitement than other species, although they have tolerated meperidine relatively well. Avoid repeated doses because accumulation of metabolites may be toxic.

**Drug Interactions**

Meperidine should not be administered with monoamine oxidase inhibitors (MAOIs), such as selegiline. Meperidine and metabolites may inhibit reuptake of serotonin and cause excess serotonin effect, especially if combined with other drugs that produce similar action, such as selective serotonin reuptake inhibitors (e.g., fluoxetine), tricyclic antidepressants (e.g., clomipramine), or other analgesics such as tramadol.

## Instructions for Use

Although comparative clinical studies have not been conducted in animals, meperidine may be effective for short duration, but has not been used for long-term pain management.

## Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

## Formulations

- Meperidine is available in 50- and 100-mg tablets; 10-mg/mL syrup; and 25-, 50-, 75-, and 100-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water. It may be mixed with 0.9% saline or 5% dextrose for 28 days without loss of potency or stability. It is stable in syrup formulation. Protect from freezing.

## Small Animal Dosage

### Dogs

- 5-10 mg/kg IV or IM as often as every 2-3 hours (or as needed).

### Cats

- 3-5 mg/kg IV or IM every 2-4 hours (or as needed).

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Schedule II controlled drug.

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 1

## Mepivacaine

meh-piv'ah-kane

**Trade and other names:** Carbocaine-V

**Functional classification:** Local anesthetic

## Pharmacology and Mechanism of Action

Mepivacaine is a local anesthetic of the amide class. It inhibits nerve conduction via sodium channel blockade. It has medium potency and duration of action compared to bupivacaine. Compared to lidocaine, it is longer acting but has equal potency.

## Indications and Clinical Uses

Mepivacaine is used as a local anesthetic for local infiltration epidural analgesia/anesthesia.



**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are rare with local infiltration. High doses absorbed systemically can cause nervous system signs (tremors and convulsions). After epidural administration, respiratory paralysis is possible with high doses. Mepivacaine may cause less irritation to tissues than lidocaine.

**Contraindications and Precautions**

No contraindications have been reported for animals.

**Drug Interactions**

No drug interactions have been reported.

**Instructions for Use**

For epidural use, do not exceed 8 mg/kg total dose. Duration of epidural analgesia is 2.5-3 hours.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

Mepivacaine is available in a 2% (20-mg/mL) injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs and Cats**

- Local infiltration dose varies depending on site. Generally 0.5-3 mL of 2% solution is used.
- Epidural: 0.5 mL of 2% solution q30sec until reflexes are absent.

**Large Animal Dosage****Horses**

- Intraarticular: 150 mg (7.5 mL) injected into horse joint. Other doses are variable doses used for local infiltration, depending on the need.

**Regulatory Information**

No regulatory information is available. Because of low risk of residues when used for local infiltration, no withdrawal times are suggested.

Horses: Clearance prior to racing is approximately 2 days.

RCI Classification: 2

**Mercaptopurine**

mer-kap-toe-pyoo'reen

**Trade and other names:** Purinethol

**Functional classification:** Anticancer agent

## Pharmacology and Mechanism of Action

Anticancer agent. Antimetabolite agent that inhibits synthesis of purines in cancer cells. It is cell-cycle specific and acts at the S-phase of cell division.

## Indications and Clinical Uses

Mercaptopurine is used for various forms of cancer, including leukemia and lymphoma. A related drug is azathioprine. Administration of azathioprine is metabolized to 6 mercaptopurine, which is further metabolized to cytotoxic products.

### Precautionary Information

#### Adverse Reactions and Side Effects

Many side effects are possible that are common to anticancer therapy (many of which are unavoidable), including bone marrow suppression and anemia.

#### Contraindications and Precautions

Do not use in animals with known sensitivity to azathioprine. Do not administer to cats.

#### Drug Interactions

No drug interactions are reported. It has been used with other anticancer drug protocols.

## Instructions for Use

Consult the specific anticancer protocol for specific regimen.

## Patient Monitoring and Laboratory Tests

Monitor CBC for evidence of bone marrow toxicity.

## Formulations

- Mercaptopurine is available in 50-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is prone to oxidation if mixed with alkaline solutions. pH of solutions should be below 8. If mixed with oral vehicles, such as syrups, it was stable for 14 days.

## Small Animal Dosage

### Dogs

- 50 mg/m<sup>2</sup> q24h PO.

### Cats

- Contraindicated.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Meropenem

meer-oh-pen'em

**Trade and other names:** Merrem

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Beta-lactam antibiotic of the carbapenem class (also known as penems) with broad spectrum of activity related to imipenem. Action on the cell wall is similar to other beta-lactams, which is to bind penicillin-binding proteins (PBPs) that weaken or interfere with cell wall formation. The carbapenems bind to a specific PBP (PBP-1) that results in more rapid lysis compared to other beta-lactams. This results in greater bactericidal activity and a longer postantibiotic effect. Carbapenems have a broad spectrum of activity and are among the most active of all antibiotics. Spectrum includes gram-negative bacilli, including Enterobacteriaceae and *Pseudomonas aeruginosa*. It also is active against most gram-positive bacteria, except methicillin-resistant strains of *Staphylococcus*. It is not active against *Enterococcus*. Meropenem is the most active of all beta-lactams and active against aerobic and anaerobic gram-positive and gram-negative bacteria. Other related carbapenems are doripenem, imipenem, and ertapenem.

## Indications and Clinical Uses

Meropenem is indicated primarily for resistant infections caused by bacteria resistant to other drugs. It is especially valuable for treating resistant infections caused by *P. aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*. Meropenem is slightly more active against some bacteria than imipenem.

### Precautionary Information

#### Adverse Reactions and Side Effects

Carbapenems pose similar risks as other beta-lactam antibiotics, but adverse effects are rare. Meropenem does not cause seizures as frequently as imipenem. Subcutaneous injections may cause slight hair loss at the injection site.

#### Contraindications and Precautions

Some slight yellowish discoloration may occur after reconstitution. Slight discoloration will not affect potency. However, a darker amber or brown discoloration may indicate oxidation and loss of potency.

#### Drug Interactions

Do not mix in a vial or syringe with other antibiotics.

## Instructions for Use

Doses in animals have been based on pharmacokinetic studies rather than efficacy trials. Meropenem is more soluble than imipenem and can be injected via bolus rather than administered in fluid solutions. Meropenem has been injected SQ in dogs with no evidence of tissue reaction.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are  $\leq 1$  mcg/mL. Sensitivity to imipenem can be used as a marker for meropenem.

## Formulations

- Meropenem is available in a 500-mg or 1-g vial; both produce 50 mg/mL after reconstitution for injection. Reconstitute with sodium chloride, Ringer's solution, or lactated Ringer's solution.

## Stability and Storage

Stable if stored in manufacturer's original vial. In heat and alkaline conditions, the drug may hydrolyze to meropenemic acid. At room temperature, IV solutions are stable for 12 hours. However, after reconstitution, stability studies have shown that

meropenem is stable for up to 25 days if refrigerated at a concentration of 50 mg/mL. Slight yellow discoloration may occur without loss of potency. Discard if particulates form in vial.

### Small Animal Dosage

#### Dogs

- 8.5 mg/kg SQ q12h or 24 mg/kg IV q12h.
- Urinary tract infections: 8 mg/kg q12h SQ.
- For infections caused by *P. aeruginosa* or other organisms that may have higher MIC values (e.g., MIC of 1.0 mcg/mL), administer 12 mg/kg q8h SQ or 25 mg/kg q8h IV.

#### Cats

- 10 mg/kg IM, SC, or IV, q12h.

### Large Animal Dosage

- No large animal doses have been reported. However, doses similar to the range used in small animals are suggested for foals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Mesalamine

mez-ahl'ah-meen

**Trade and other names:** 5-aminosalicylic acid, Asacol, Mesasal, Pentasa, and Mesalazine

**Functional classification:** Antidiarrheal

### Pharmacology and Mechanism of Action

Mesalamine is also known as 5-aminosalicylic acid. It is the active component of sulfasalazine, which is commonly administered for treatment of colitis. (See sulfasalazine and olsalazine for additional information.) The action of mesalamine is not precisely known, but it appears to suppress the metabolism of arachidonic acid in the intestine. It inhibits both COX- and lipoxygenase-mediated mucosal inflammation. Systemic absorption is low; most of the action is believed to be local. Four formulations of mesalamine are used:

1. Asacol. Asacol is a tablet coated with an acrylic-based resin. The resin dissolves at a pH of 7.0 and is designed to release 5-aminosalicylic acid in the colon.
2. Mesasal. Mesasal is a tablet coated with an acrylic-based resin that dissolves at a pH of >6.0. It is designed to release 5-aminosalicylic acid in the terminal ileum and colon. Approximately 35% of the salicylate is absorbed systemically. The dose in people is 1-1.5 g/day.
3. Olsalazine sodium (Dipentum). Olsalazine is a dimer of two molecules of 5-aminosalicylic acid linked by an azo bond that is released by bacterial digestion in the colon. It is used in people who cannot tolerate sulfasalazine. Only 2% of the salicylate from this compound is absorbed systemically. The most common adverse effect in people from this preparation has been watery diarrhea.
4. Pentasa. Pentasa contains microgranules of mesalamine coated with ethyl cellulose, which releases 5-aminosalicylic acid into the small and large intestine gradually, regardless of pH.

## Indications and Clinical Uses

Mesalamine is used for treatment of inflammatory bowel disease, including colitis, in animals. Most often sulfasalazine is used; however, in some animals, especially those sensitive to sulfonamides, mesalamine may be indicated. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

Mesalamine alone has not been associated with side effects in animals. Adverse effects associated with sulfasalazine are caused by the sulfonamide component. (See sulfasalazine for more information.)

#### Contraindications and Precautions

Drug interactions are possible, but they have not been reported in animals, probably because low systemic drug levels are achieved. Mesalamine, if absorbed sufficiently, can potentially interfere with thiopurine methyltransferase and, therefore, increase the risk of toxicity from azathioprine.

#### Drug Interactions

No drug interactions are reported in animals. Omeprazole can potentially increase absorption by increasing intestinal pH.

## Instructions for Use

Mesalamine usually is used as a substitute for sulfasalazine in animals that cannot tolerate sulfonamides.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Mesalamine is available in 400-mg tablets and 250-mg capsules. Delayed-release tablets are 400 mg (Asacol) and 1.2 g (film-coated Lialda). Controlled-release capsules are 250 and 500 mg (ethylcellulose-coated Pentasa).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is slightly soluble in water and ethanol. It should be protected from air and moisture. Darkening may occur after exposure to air. Do not crush coated tablets.

## Small Animal Dosage

- Veterinary dose has not been established. The usual human dose is 400-500 mg q6-8h PO, and it has been used to extrapolate an animal dose (e.g., 5-10 mg/kg q8h PO).

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

RCI Classification: 5

## Metaflumizone

met-ah' floo-mah-zone

**Trade and other names:** ProMeris

**Functional classification:** Antiparasitic

This product has been removed from the market. Consult previous editions of this handbook for information on pharmacology and clinical use.

## Metaproterenol Sulfate

met-ha-proe-teer'eh-nole sul'fate

**Trade and other names:** Alupent, Metaprel, and Orciprenaline sulphate

**Functional classification:** Bronchodilator, beta-agonist

### Pharmacology and Mechanism of Action

Beta<sub>2</sub>-adrenergic agonist. Bronchodilator. Like other beta<sub>2</sub> agonists, it stimulates beta<sub>2</sub> receptors, activates adenylyl cyclase, and relaxes bronchial smooth muscle. It also may inhibit release of inflammatory mediators, especially from mast cells. Pharmacokinetics have not been well studied in the veterinary species. In people, it is well absorbed from oral administration, but information on oral absorption in animals is incomplete.

### Indications and Clinical Uses

Metaproterenol is used in animals to relax bronchial smooth muscle to treat bronchitis, obstructive pulmonary disease, airway obstruction caused by inflammation, and other airway diseases. It is indicated in animals with reversible bronchoconstriction, such as cats with bronchial asthma. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

Metaproterenol causes excessive beta-adrenergic stimulation at high doses (tachycardia and tremors). Arrhythmias occur at high doses or in sensitive individuals. Beta-agonists will inhibit uterine contractions in animals in labor.

#### Contraindications and Precautions

Use cautiously in animals with cardiac disease.

#### Drug Interactions

Do not administer with monoamine oxidase inhibitors (MAOI). Use cautiously with other drugs that may cause cardiac arrhythmias in animals. It may be mixed with cromolyn sodium for nebulization if used within 60-90 minutes. It also has been combined with dexamethasone without loss of stability.

### Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

## 500 **Metformin**

Beta<sub>2</sub> agonists also have been used in people to delay labor (inhibit uterine contractions).

### **Patient Monitoring and Laboratory Tests**

Monitor heart rate and rhythm of animals during treatment.

### **Formulations**

- Metaproterenol is available in 10- and 20-mg tablets, 5-mg/mL syrup, and inhalers.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Avoid exposure to air and moisture. Do not freeze. Do not use if formulation turns dark color.

### **Small Animal Dosage**

#### **Dogs and Cats**

- 0.325-0.65 mg/kg q4-6h PO.

### **Large Animal Dosage**

- No large animal doses have been reported. There is no evidence of oral absorption in large animals.

### **Regulatory Information**

Do not administer to animals that produce food. Other beta-agonists (clenbuterol) are banned for use in food animals.

RCI Classification: 3

## **Metformin**

met-for'min

**Trade and other names:** Glucophage

**Functional classification:** Antihyperglycemic

### **Pharmacology and Mechanism of Action**

Metformin is an oral antihyperglycemic agent used to treat noninsulin-dependent diabetes (type 2 diabetes in people). Metformin is used to decrease hepatic glucose production, decrease intestinal absorption of glucose, and improve insulin sensitivity by increasing peripheral glucose uptake and utilization. It is in the biguanide class of oral drugs for diabetes. Metformin does not have a direct effect on pancreatic beta cells, but it lowers blood glucose by reducing hepatic glucose production and improving peripheral utilization of glucose (e.g., in muscle). It thus lowers insulin requirements without any direct effect to increase insulin secretion. It may increase the insulin receptors on tissues. At therapeutic doses, metformin will not cause hypoglycemia. Half-life in cats is 2.75 hours.

### **Indications and Clinical Uses**

In people, metformin is used to treat type 2 diabetes. It has been used in people when the sulfonylurea drugs fail. It has been used in cats to treat diabetes. However, in cats treated with 50 mg/cat q12h PO, it showed significant adverse effects and was effective in only one fifth of treated cats. In cats, it has been more common to administer the sulfonylurea class of drugs. Sulfonylurea drugs include glipizide

(Glucotrol) and glyburide (DiaBeta, Micronase). Diabetic dogs rarely respond to oral hypoglycemic agents. It has been considered for treatment of insulin resistance in horses and ponies, but the bioavailability is very low in horses compared to that of humans and, because of poor oral bioavailability, it is not recommended.

### Precautionary Information

#### Adverse Reactions and Side Effects

Metformin has caused lethargy, appetite loss, vomiting, and weight loss in cats. Use has not been common enough to document other effects. However, in people, it has caused lactic acidosis in some patients, which was serious. Metformin also has caused megaloblastic anemia by affecting vitamin B<sub>12</sub> absorption.

#### Contraindications and Precautions

Metformin is cleared by the kidneys, so doses will need to be adjusted in patients with renal failure.

#### Drug Interactions

Use cautiously with drugs that may affect glycemic control such as glucocorticoids.

### Instructions for Use

Doses published for cats are based on pharmacokinetic studies that demonstrated oral absorption in cats to be 35%-70%. The half-life was 11.5 hours, which is the basis for the q12h dosage recommendation.

### Patient Monitoring and Laboratory Tests

Blood glucose should be monitored carefully. Doses should be adjusted on the basis of glucose monitoring. Some animals may require insulin injections to control hyperglycemia.

### Formulations Available

- Metformin is available in 500- and 850-mg tablets.

### Stability and Storage

Stable if maintained in original formulation.

### Small Animal Dosage

#### Cats

- 25 or 50 mg/cat q12h PO (5-10 mg/kg q12h). (Efficacy is limited.)

### Large Animal Dosage

- Because of high clearance and poor bioavailability in horses (4%-7%), its use is not recommended.

### Regulatory Information

Do not administer to animals intended for food.

## Methadone Hydrochloride

meth'ah-done hye-droe-klor'ide

**Trade and other names:** Dolophine, Methadose, and generic brands

**Functional classification:** Analgesic, opioid



## **Pharmacology and Mechanism of Action**

Opioid agonist, analgesic. Action of methadone is to bind to mu-opiate and kappa-opiate receptors on nerves and inhibit release of neurotransmitters involved with transmission of pain stimuli (such as substance P). Methadone also may antagonize n-methyl D-aspartate (NMDA) receptors, which may contribute to the analgesic effect, decrease adverse CNS effects, and inhibit tolerance. Methadone exists in two forms: levomethadone and dextromethadone. Levomethadone, which is available in some countries, has higher affinity for opiate receptors and has been available in a 2.5-mg/mL solution combined with 0.125 mg per mL fenpipramide (an anticholinergic agent). Other opiates used in animals include morphine, hydromorphone, codeine, oxymorphone, meperidine, and fentanyl.

Pharmacokinetics have been studied in horses, cats, and dogs. In all species studied, oral absorption is either too low or variable to use this as a method of administration. In horses, the oral absorption was 30% from intragastric administration, but 3 times higher from oral administration. (Absorption may occur from the oral mucosa in horses.) The half-life in all species is short. In horses, it is approximately 1-2 hours. In dogs, the half-life is 2-4 hours with clearance of 30 mL/kg/min.

## **Indications and Clinical Uses**

Most of the use in veterinary medicine to document the efficacy and safety of methadone is based on anecdotal experience, a few efficacy studies, and some pharmacokinetic studies. However, there is an approved formulation in Europe with controlled studies to support efficacy.

Methadone is indicated for short-term analgesia, for sedation, and as an adjunct to anesthesia. It is compatible with most anesthetics and can be used as part of a multimodal approach to analgesia/anesthesia. Administration of methadone may lower dose requirements for other anesthetics and analgesics used. Oral doses to dogs are not absorbed systemically. Oral mucosal (buccal) administration to dogs is not practical, but oral mucosal administration to cats may be considered (absorption 44%). Duration of analgesia in cats is 2-4 hours and as long as 6-8 hours.

## **Precautionary Information**

### **Adverse Reactions and Side Effects**

Like all opiates, side effects from methadone are predictable and unavoidable. However, some side effects such as excitement and dysphoria seen with other opiates have not been as common with methadone in dogs and cats. Side effects from methadone administration may include sedation, vomiting, constipation, urinary retention, and bradycardia. Panting may occur in dogs as a result of changes in thermoregulation. Effects such as excitement and dysphoria have not been observed with administration of methadone as much as some of the other opiates. In dogs, IV administration produced less dysphoria and excitement compared to other opiates. In horses, IV administration did not produce behavior changes, sedation, increased locomotion, or decreased intestinal motility. Oral doses up to 0.4 mg/kg in horses did not produce adverse reactions.

### **Contraindications and Precautions**

Methadone is a Schedule II controlled substance. Cats may be more sensitive to excitement than other species, but this has not been examined for methadone.

### **Drug Interactions**

Chloramphenicol, and possibly other drugs, will decrease clearance and increase plasma concentrations of methadone in dogs.

## Instructions for Use

Oral doses have not been absorbed in dogs. Effective dose has not been established for horses, but oral administration of 0.1 to 0.4 mg/kg has been administered without adverse effects, and produced drug concentrations in the effective range.

## Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone. Although plasma concentrations are not typically monitored, the range of concentrations considered therapeutic in people is 33-60 ng/mL.

## Formulations

- Methadone is available in 1- and 2-mg/mL oral solution; 5-, 10-, and 40-mg tablets; and 10-mg/mL injectable solution. There is a licensed formulation of methadone for cats available in some European countries.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water and ethanol. It may precipitate from a solution if pH is higher than 6. It has been combined in oral mixtures with juices and syrups and remained stable for at least 14 days.

## Small Animal Dosage

### Dogs

- 0.1-0.5 mg/kg IV, or 0.5-2.2 mg/kg q3-4h SQ or IM.

### Cats

- 0.3-0.6 mg/kg q3-4h IV, SQ, or IM. Cats have tolerated doses up to 0.6 mg/kg IM, with a 4-hour duration of activity.
- Oral mucosal administration is approximately 2 times the IV dose because of less than 50% absorption.

## Large Animal Dosage

### Horses

- 0.15 mg/kg IV, or Oral q6-8h.

## Regulatory Information

Do not administer to animals intended for food.

Methadone is a Schedule II controlled drug.

RCI Classification: 1

## Methazolamide

meth-ah-zole'ah-mide

**Trade and other names:** Neptazane

**Functional classification:** Diuretic

## Pharmacology and Mechanism of Action

Methazolamide is a carbonic anhydrase inhibitor. Methazolamide, like other carbonic anhydrase inhibitors, produces diuresis through inhibition of the uptake of bicarbonate in proximal renal tubules via enzyme inhibition. This action results in loss of bicarbonate in the urine and diuresis. The action of carbonic anhydrase inhibitors

results in urine loss of bicarbonate, alkaline urine, and water loss. Methazolamide, like other carbonic anhydrase inhibitors, also decreases formation of cerebrospinal fluid (CSF) by the choroid plexus and decreases the ocular fluid formation by decreasing bicarbonate secretion by the ocular ciliary body. This effect on aqueous humor formation decreases ocular pressure.

### **Indications and Clinical Uses**

Methazolamide is rarely used as a diuretic any longer. More potent and effective diuretic drugs are available, such as the loop diuretics (furosemide). Methazolamide, like other carbonic anhydrase inhibitors, is used primarily to lower intraocular pressure in animals with glaucoma. Its duration is relatively short in dogs, in which more frequent administration may be required to maintain low ocular pressure. Methazolamide is used more often than acetazolamide for this purpose because it is more effective and easily available. However, other regimens are commonly used for the treatment of glaucoma compared to the carbonic anhydrase inhibitors. Methazolamide, like other carbonic anhydrase inhibitors, is sometimes used to produce more alkaline urine for management of some urinary calculi.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Methazolamide may produce hypokalemia in some patients. Like other carbonic anhydrase inhibitors, it can produce significant bicarbonate loss, and patients should be supplemented with bicarbonate if repeated doses are administered.

#### **Contraindications and Precautions**

Do not use in patients with acidemia. Use cautiously in any animal sensitive to sulfonamides. Do not use in patients with hepatic encephalopathy.

#### **Drug Interactions**

Use cautiously with other treatments that could cause metabolic acidosis.

### **Instructions for Use**

Methazolamide may be used with other glaucoma agents, such as topical drugs to decrease intraocular pressure, and it may be used to produce alkaline urine to prevent some calculi from forming. However, use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### **Patient Monitoring and Laboratory Tests**

Monitor ocular pressure in treated patients. Monitor urine pH if it is used to produce alkaline urine. Monitor electrolyte and acid-base status if multiple doses are administered.

### **Formulations Available**

- Methazolamide is available in 25- and 50-mg tablets.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### **Small Animal Dosage**

#### **Dogs and Cats**

- 2-3 mg/kg q8-12h PO. There does not seem to be any benefit for increasing the dose to a maximum dose of 4-6 mg/kg, but more frequent administration (every 8 hours) may be beneficial.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 4

## Methenamine

meth-en'ah-meen

**Trade and other names:** Methenamine hippurate: Hiprex and Urex; Methenamine mandelate: Mandelamine and generic brands

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Methenamine is a urinary antiseptic. In the acid environment of the urine, methenamine is hydrolyzed to formaldehyde and ammonia to produce an antibacterial/antifungal effect. A low urine pH of 5.5 or less is needed for optimal effect. If this can be achieved, it is active against a wide range of bacteria and resistance does not develop. It is less effective against *Proteus* species that produce an alkaline urine pH. Because there is no systemic absorption, it is not effective for systemic infections. Absorption is rapid and produces a peak effect in urine at 0.5-1.5 hours and has a half-life of 3-6 hours.

M

## Indications and Clinical Uses

Methenamine is used as a urinary antiseptic. There is a lack of well-controlled clinical trials to show its effectiveness. However, it has been used in animals to prevent recurrences of lower UTIs. It is probably less effective for treating ongoing infections. It is critical that the urine pH be low for conversion to formaldehyde.

## Precautionary Information

### Adverse Reactions and Side Effects

Although formaldehyde formation in bladder may be irritating, in people, high doses were required (greater than 8 g/day). In animals, no adverse effects have been reported.

### Contraindications and Precautions

High doses may irritate bladder mucosa. Do not administer with sulfonamides because it may form formaldehyde-sulfonamide complexes. Do not use the mandelate formulation in patients with renal insufficiency.

### Drug Interactions

Do not administer with medications that may cause alkaline urine. Because methenamine is often administered with urine acidifiers, acid urine will decrease the activity of fluoroquinolone and aminoglycoside antibiotics. Methenamine can combine in the urine with sulfonamide drugs to produce antagonism. The tablets should be enteric coated to protect from hydrolysis in the acid of the stomach and should be administered on an empty stomach.

## Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals is based on experience in people or anecdotal experience in animals. Urine must be acidic for

methenamine to convert to formaldehyde (monitor pH periodically). A pH <5.5 is optimal. Supplement with ascorbic acid or ammonium chloride to lower pH.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. Monitor urinalysis or culture of urine to guide therapy of UTI.

### Formulations

- Methenamine hippurate is available in 0.6-g and 1-g tablets. Methenamine mandelate is no longer available (previous formulations included 1-g tablets, granules for oral solution, and 50- and 100-mg/mL oral suspension).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Methenamine is soluble in water and ethanol. In an acidic environment, it is hydrolyzed to form formaldehyde and ammonia. It has been physically incompatible when mixed with some foods and suspensions.

### Small Animal Dosage

#### Dogs

- Methenamine hippurate: 500 mg/dog q12h PO.
- Methenamine mandelate (if available): 10-20 mg/kg q8-12h PO.

#### Cats

- Methenamine hippurate: 250 mg/cat q12h PO.
- Methenamine mandelate (if available): 10-20 mg/kg q8-12h PO.

### Large Animal Dosage

- No large animal doses have been reported. It is unlikely to be effective in large animals because their urine is more alkaline.

### Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

## Methimazole

meth-im'ah-zole

**Trade and other names:** Tapazole, Felimazole, Thiamazole, and generic.

**Functional classification:** Antithyroid agent

### Pharmacology and Mechanism of Action

Antithyroid drug. Action is to serve as substrate for thyroid peroxidase (TPO), to inhibit it and decrease incorporation of iodide into tyrosine molecules for the formation of thyroxine ( $T_4$ ) and triiodothyronine ( $T_3$ ). Methimazole inhibits coupling of monoiodinated and di-iodinated residues to form  $T_4$  and  $T_3$ . Methimazole does not inhibit release of preformed thyroid hormone. It does not affect existing thyroid hormones already circulating or stored in the thyroid gland and does not inhibit the peripheral conversion of  $T_4$  to  $T_3$ . It generally takes 2 to 4 weeks for serum  $T_4$  to reach the normal range in hyperthyroid cats treated with methimazole. Carbimazole is a similar drug used in Europe that is converted to methimazole in animals. Methimazole also may

have immunosuppressive effects. Treatment may decrease antithyrotropin-receptor antibodies. Methimazole has a half-life of 2.3-3.1 hours in hyperthyroid cats and 4.7 hours in normal cats. Oral absorption in cats is high (93%).

## Indications and Clinical Uses

Methimazole is used to treat hyperthyroidism in animals, especially cats. There is good evidence for efficacy when administered to cats at recommended doses. Methimazole is preferred in cats instead of propylthiouracil (PTU) because methimazole has a lower incidence of adverse effects. Evidence supports twice-daily dosing in cats as more effective than once daily. Methimazole has been formulated for use in cats as a transdermal gel for skin absorption (e.g., those combined with pluronic organogel [PLO] gel or based in a lipid vehicle). These formulations are available through compounding pharmacies. Published data indicate that transdermal methimazole is not as rapidly acting or as effective as oral dosing, but it can be effective to reduce  $T_4$  concentrations in many cats. At a dose of 5 mg/kg per cat transdermal, the concentrations may not be adequate for cats, but 10 mg per cat was more effective. An alternative oral drug that has been used is carbimazole, which is converted to the active drug methimazole. It may produce less frequent gastrointestinal problems. However, experience with carbimazole is limited in the US (see carbimazole for more details).

## Precautionary Information

### Adverse Reactions and Side Effects

In cats, gastrointestinal problems are the most common and can include anorexia and vomiting. Most adverse effects caused by methimazole are dose related and can be decreased by lowering the dose. In cats, polyarthritis, alopecia, and scaling and crusting of the head and face have been observed, which may be a manifestation of an allergic reaction. In cats, lupuslike reactions are possible, such as vasculitis and bone marrow changes. In cats, abnormal platelet counts and low blood counts can develop after 1-3 months of treatment. Bleeding abnormalities may be related to thrombocytopenia, but tests conducted in cats did not demonstrate prolongation of bleeding times (prothrombin time and activated partial thromboplastin time). There were fewer adverse gastrointestinal effects when methimazole was applied as a transdermal gel compared to administration as an oral tablet. Methimazole treatment may unmask hypothyroidism and renal failure in some cats. Monitor renal function with continued treatment.

### Contraindications and Precautions

Do not administer to animals with thrombocytopenia or bleeding problems. Other drugs, such as beta blockers, are safe to administer with methimazole. Warn pet owners that transdermal methimazole can be absorbed through human skin. If an animal has had an adverse reaction to PTU, there may also be cross-sensitivity to methimazole. Methimazole has caused fetal abnormalities and should not be used in pregnant animals.

### Drug Interactions

There are no drug interactions reported from the use in animals.

## Instructions for Use

Use in cats is based on clinical studies in hyperthyroid cats and information from the feline drug sponsor. Methimazole has, for the most part, replaced PTU for use in cats. Adjust maintenance dose by monitoring thyroid ( $T_4$ ) concentrations in plasma. Because it does not inhibit release of preformed thyroid, it may take 2-4 weeks to

achieve maximum effect. A study that evaluated dosing frequency found that 5 mg/kg q12h PO was more effective than 5 mg/kg q24h, PO.

*Transdermal gel use in cats:* Methimazole has also been prepared as a transdermal gel by compounding pharmacies. If compounded as a transdermal gel, the recommended final concentration is 5 mg/0.1 mL of transdermal gel applied to the inner ear. There are also transdermal products prepared in lipid vehicles. Transdermal gel may be less effective than oral tablets. Efficacy may be caused by cats licking medication from their paws after rubbing ears. Although transdermal methimazole may be a safe and effective alternative for long-term use in some cats, there is high variability in the thyroid concentrations in treated cats, and it may be difficult to keep the  $T_4$  consistently within the reference range. The transdermal dose of 5 mg per cat once daily appears to be as effective as 2.5 mg per cat twice daily.

### **Patient Monitoring and Laboratory Tests**

Monitor serum  $T_4$  levels. Recheck  $T_4$  levels after first month of treatment. Whether the concentration was measured before dosing or during the dose interval did not affect the  $T_4$  concentration. After methimazole treatment is stabilized,  $T_3$  and  $T_4$  are suppressed for 24 hours after each dose of methimazole. Therefore timing of blood sample after oral methimazole in cats does not appear to be a significant factor when assessing response to treatment. Thyroid-stimulating (TSH) concentrations in cats may also be used to test effectiveness of treatment. (Feline TSH has 96% homology with canine TSH.) Monitor CBC and platelet count in cats every week or 14 days for the first 30 days of treatment. Monitor tests of renal function because of concern about increased risk of renal disease in some cats. Monitor liver enzymes before and during treatment. Some cats with hyperthyroidism also have elevated liver enzymes. Methimazole may affect thyroid scintigraphy tests. After treatment, there may be a stimulation from TSH for tissues to have enhanced uptake of  $^{99m}\text{TcO}_4$  by the thyroid gland.

### **Formulations**

- Methimazole is available in 2.5- and 5-mg coated tablets (veterinary form) and 5- and 10-mg tablets (human form). There are no approved transdermal formulations for cats in the US.

### **Stability and Storage**

Methimazole is stable if maintained in its original formulation. However, if prepared in compounded formulations for cats, potency and stability may be less. Potency is assured for 2 weeks with compounded transdermal gel.

### **Small Animal Dosage**

#### **Cats**

- 2.5 mg/cat q12h PO for 7-14 days, then adjust dose to 5-10 mg/cat PO q12h as needed. Monitor  $T_4$  concentrations and adjust dose accordingly.
- Transdermal dose: 2.5 mg per/cat transdermally twice daily or 5 mg per cat once daily. Alternate ears with each dose, and wear gloves when applying. If 5 mg per cat per day is not effective, a dose of 10 mg per cat per day may improve response.

### **Large Animal Dosage**

- No large animal doses have been reported.

### **Regulatory Information**

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food.

## Methocarbamol

meth-oh-kar'bah-mole

**Trade and other names:** Robaxin-V

**Functional classification:** Muscle relaxant

### Pharmacology and Mechanism of Action

Skeletal muscle relaxant. Methocarbamol depresses polysynaptic reflexes to cause muscle relaxation.

### Indications and Clinical Uses

Methocarbamol has been used for the treatment of skeletal muscle spasms and increased muscle tone. It has also been used to treat pain that is associated with increased muscle spasms or myositis. Higher doses than listed in the dosing section are recommended if it is used for treating tetanus. However, evidence for efficacy in animals is lacking. For some indications (e.g., muscle spasms), methocarbamol has been replaced by other muscle relaxants such as orphenadrine (Norflex). In horses, the half-life is only 60-90 minutes and may need frequent administration for effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

Methocarbamol may cause depression and sedation of the CNS. Excess salivation, emesis, weakness, and ataxia have been observed from methocarbamol administration. Adverse effects are usually short in duration.

#### Contraindications and Precautions

Use cautiously with other drugs that depress the CNS.

#### Drug Interactions

No drug interactions reported for animals.

### Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Methocarbamol is available in 500- and 750-mg tablets and 100-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 44 mg/kg q8h PO or IV on the first day, and then 22-44 mg/kg q8h PO. Up to 130 mg/kg for severe conditions.



## Large Animal Dosage

- 11-22 mg/kg q8h IV or more frequently if needed. In horses, higher doses of 30 mg/kg IV and 50-100 mg/kg PO have been administered but are more likely to produce mild-to-moderate depression.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use with withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Methohexital Sodium

meth-oe-heks'ih-tahl soe'dee-um

**Trade and other names:** Brevital

**Functional classification:** Anesthetic, barbiturate

## Pharmacology and Mechanism of Action

Barbiturate anesthetic. Methohexital is an oxybarbiturate that it is ultra-short acting. Methohexital is twice as potent as thiopental, but has a higher incidence of CNS excitatory effects. Anesthesia is produced by CNS depression without analgesia. Anesthesia is terminated by redistribution in the body.

## Indications and Clinical Uses

Methohexital is used as an IV anesthetic in animals, given either as a bolus or CRI. Frequently other anesthetic adjuncts, such as tranquilizers, are administered prior to methohexital infusion.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are related to the anesthetic effects of the drug. Severe adverse effects are caused by respiratory and cardiovascular depression.

### Contraindications and Precautions

Overdoses can be caused by rapid or repeated injections. Avoid extravasation outside of the vein.

### Drug Interactions

No drug interactions have been reported for animals.

## Instructions for Use

Therapeutic index is low. Use only in patients in which it is possible to monitor cardiovascular and respiratory functions. Methohexital is often administered with other anesthetic adjuncts.

## Patient Monitoring and Laboratory Tests

Monitor heart rate and breathing in patients anesthetized with barbiturates.

## Formulations

- Methohexital is available in 0.5-, 2.5-, and 5-g vials for injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 3-6 mg/kg IV (give slowly to effect). Doses as high as 15 mg/kg IV have been administered to dogs over 30 seconds.
- CRI: 0.25 mg/kg/min for 30 minutes, then 0.125 mg/kg/min.

## Large Animal Dosage

- **Horses:** 5 mg/kg IV (to effect).
- **Pigs:** 5-8 mg/kg IV (to effect).

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).  
Schedule III controlled drug  
RCI Classification: 2

## Methotrexate

meth-oh-treks'ate

**Trade and other names:** MTX, Mexate, Folex, Rheumatrex, and generic brands

**Functional classification:** Anticancer agent

M

## Pharmacology and Mechanism of Action

Anticancer agent. Action is via antimetabolite action. The structure of methotrexate is similar to folic acid, and methotrexate binds and inhibits the dihydrofolate reductase (DHFR) enzyme. The DHFR enzyme is a reducing enzyme necessary for purine synthesis. The reduced form of folic acid (tetrahydrofolate [FH<sub>4</sub>]) acts as an important coenzyme for biochemical reactions, particularly DNA, RNA, and protein synthesis.

## Indications and Clinical Uses

Methotrexate is used for various carcinomas, leukemia, and lymphomas. In people, methotrexate is also commonly used for autoimmune diseases such as rheumatoid arthritis. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

## Precautionary Information

### Adverse Reactions and Side Effects

The important adverse effects in animals are anorexia, nausea, myelosuppression, and vomiting. Anticancer drugs cause predictable (and sometimes unavoidable) side effects that include bone marrow suppression, leukopenia, and immunosuppression. Hepatotoxicity has been reported in people from methotrexate therapy, but this has not been documented in veterinary medicine. In people, higher doses are often used compared to veterinary doses. In people, risk of systemic toxicity is high, and rescue therapy with leucovorin (tetrahydrofolic acid) is often used (also called calcium folinate). Leucovorin rescue therapy is used because it is an antagonist of the action of methotrexate on the DHFR enzyme. Dose range of leucovorin in dogs is 25-200 mg/m<sup>2</sup> every 6 hours, depending on plasma methotrexate concentration. Another approach is to administer a dose of leucovorin that is equal to the dose of methotrexate.

**Contraindications and Precautions**

Do not administer to pregnant animals. It has been used to induce abortion.

**Drug Interactions**

Concurrent use with NSAIDs may cause severe methotrexate toxicity. Do not administer with penicillins, fluoroquinolones, pyrimethamine, trimethoprim, sulfonamides, or other drugs that may affect folic acid synthesis.

**Instructions for Use**

Use in animals has been based on experimental studies. Only limited clinical information is available. Consult specific anticancer protocols for precise dosage and regimen.

**Patient Monitoring and Laboratory Tests**

Monitor CBC for evidence of bone marrow toxicity.

**Formulations**

- Methotrexate is available in 2.5-mg tablets and 2.5- and 25-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs and Cats**

- 2.5-5 mg/m<sup>2</sup> q48h PO (dose depends on specific cancer protocol).
- 0.3-0.5 mg/kg every week IV.

**Cats**

- 0.8 mg/kg IV every 2-3 weeks.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent. RCI Classification: 4

**Methoxamine**

meh-thahk'seh-meen

**Trade and other names:** Vasoxyl

**Functional classification:** Vasopressor

**Pharmacology and Mechanism of Action**

Alpha<sub>1</sub>-adrenergic agonist. Methoxamine stimulates alpha<sub>1</sub>-receptors on vascular smooth muscle to produce vasoconstriction in vascular beds.

**Indications and Clinical Uses**

Methoxamine is used primarily in patients in need of critical care or during anesthesia to increase peripheral resistance and blood pressure. There is little experience with this drug in veterinary medicine.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are related to excessive stimulation of  $\alpha_1$ -receptors (prolonged peripheral vasoconstriction). Reflex bradycardia may occur.

### Contraindications and Precautions

Use cautiously in animals with heart disease.

### Drug Interactions

Do not use with MAOIs, such as selegiline.

## Instructions for Use

Methoxamine has a rapid onset and short duration of action.

## Patient Monitoring and Laboratory Tests

Monitor heart rate and blood pressure in treated patients.

## Formulations

- Methoxamine is no longer available on the US market. Some solutions have been compounded. It was previously available as a 20-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 200-250 mcg/kg (0.2-0.25 mg/kg) IM or 40-80 mcg/kg IV; repeat dose as needed.

## Large Animal Dosage

### Cattle and Horses

- 100-200 mcg/kg (0.1-0.2 mg/kg) IM once or as needed.

## Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

## Methoxyflurane

meh-thahk'seh-floo'rane

**Trade and other names:** Metofane

**Functional classification:** Anesthetic, inhalant

## Pharmacology and Mechanism of Action

Inhalant anesthetic. Like other inhalant anesthetics, the mechanism of action is uncertain. They produce generalized, reversible depression of the CNS. The inhalant anesthetics vary in their solubility in blood, their potency, and the rate of induction and recovery. Those with low blood/gas partition coefficients are associated with the most rapid rates of induction and recovery.

## 514 Methylene Blue 0.1%

### Indications and Clinical Uses

Methoxyflurane is not used often as an inhalant anesthetic. In the past 10 years, use has declined and been replaced by other agents.

#### Precautionary Information

##### Adverse Reactions and Side Effects

Adverse effects are related to anesthetic effects (e.g., cardiovascular and respiratory depression). Methoxyflurane has been reported to cause hepatic injury in animals.

##### Contraindications and Precautions

Use cautiously in animals with cardiac disease.

##### Drug Interactions

Labeling recommendations in some countries state that flunixin should not be administered to animals receiving methoxyflurane anesthesia.

### Instructions for Use

Use of inhalant anesthetics requires careful monitoring. Dose is determined by depth of anesthesia.

### Patient Monitoring and Laboratory Tests

Monitor heart rate and breathing in patients undergoing anesthesia with inhalant anesthetics. Monitor hepatic enzymes.

### Formulations

- Methoxyflurane is currently not available through commercial sources. It was previously available as a 4-oz bottle for inhalation.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

- Induction: 3%; maintenance: 0.5%-1.5%.

### Large Animal Dosage

- Minimum alveolar concentration (MAC) value is 0.2%-0.3%.

### Regulatory Information

No withdrawal times are established for animals intended for food. Clearance is rapid, and short withdrawal times are suggested. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Methylene Blue 0.1%

meth'ih-leen bloo

**Trade and other names:** New Methylene Blue and generic brands

**Functional classification:** Antidote

### Pharmacology and Mechanism of Action

Methylene blue acts as a reducing agent to reduce methemoglobin to hemoglobin. The action of methylene blue is particularly important when it is used to convert

methemoglobin to hemoglobin in erythrocytes. It is reduced to leucomethylene blue in the body by combining with reduced nicotinamide adenine dinucleotide phosphate (NADPH) in the presence of NADPH reductase. Leucomethylene blue then transfers an electron to reduce methemoglobin to hemoglobin. Methemoglobin occurs as the result of oxidative damage to hemoglobin, and methylene blue has been used as an antidote for intoxication. Sources of intoxication in animals that cause methemoglobinemia include exposure to nitrate, nitrite, or chlorate in ruminants; acetaminophen and naphthalene (mothballs) in cats (and occasionally dogs); and local anesthetics, such as benzocaine, in cats. For acetaminophen toxicity in cats, acetylcysteine may provide a better response.

## Indications and Clinical Uses

Methylene blue is used to treat methemoglobinemia caused by chlorate and nitrate toxicosis. It also has been used to treat cyanide toxicosis.

### Precautionary Information

#### Adverse Reactions and Side Effects

In cats and dogs, administration of methylene blue to treat methemoglobinemia can cause oxidative damage to erythrocytes, including Heinz bodies, limiting the dose that can be used therapeutically. At the doses listed here, it has been safe. Heinz bodies can increase in cats from methylene blue treatment without producing anemia.

#### Contraindications and Precautions

The dose listed may produce some oxidative damage to erythrocytes (Heinz bodies and other morphologic changes) that is typically subclinical, but a risk of red cell damage and subsequent anemia increases with repeated or higher dosing. Use cautiously in cats.

#### Drug Interactions

Methylene blue is a reversible monoamine oxidase inhibitor (MAOI). If administered with drugs that affect serotonergic mechanisms or increase serotonin, it can lead to serotonin syndrome (muscle twitching, sweating, increased temperature, shivering).

## Instructions for Use

For treating acetaminophen intoxication in cats, acetylcysteine produced the best response, but methylene blue also was helpful.

## Patient Monitoring and Laboratory Tests

Monitor CBC in patients treated with methylene blue. Monitor mucous membrane color (methemoglobinemia turns the blood and membranes a chocolate color).

## Formulations

- There are no commercial veterinary methylene blue products for systemic use. The human product (1% solution, 10 mg/mL) may be appropriate for use in some species, but treatment in large animals may require a compounded formulation.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- 1.5 mg/kg IV once slowly.

## Large Animal Dosage

### Cattle, Goats, Sheep

- 4-10 mg per kg IV as needed. This dose of methylene blue should be administered, within 15 minutes. After the initial dose, lower doses may be repeated to titrate to clinical response. Higher doses may be repeated every 6-8 hours if needed. Higher doses are used for severe toxicity (15-20 mg/kg).

## Regulatory Information

Cattle withdrawal time (meat): 14 days.

Cattle withdrawal time (milk): 4 days.

## Methylnaltrexone Bromide

meth'ihl nal-trex-own broe'-mide

**Trade and other names:** Relistor

**Functional classification:** Prokinetic agent, intestinal stimulant

## Pharmacology and Mechanism of Action

Methylnaltrexone is a modified quarternary form of naltrexone that has opiate-antagonist properties. Because it is modified from naltrexone and charged, it does not cross the blood-brain barrier and it has no centrally acting opiate inhibition, but it will antagonize peripheral mu-receptors in the intestine to restore motility after postsurgical ileus. Opiate mu-receptors in the intestine ordinarily inhibit motility when stimulated because of pain or opioid drug administration. Another drug related to methylnaltrexone and used for similar purposes is alvimopan (Entereg). It has not been studied in most animal species, but in horses, it had a short half-life of 47 minutes and volume of distribution of 0.24 L/kg.

## Indications and Clinical Uses

Methylnaltrexone is approved for use in people to restore intestinal motility after surgery, after opiate administration, or when caused by a disorder (e.g., severe pain) that has stimulated mu-opiate receptors in the intestine. Use in animals is limited and has been primarily derived from empirical use. The only studies available are in horses in which methylnaltrexone increased fecal weight and prevented the effects of morphine on gastrointestinal motility. However, at the dose studied (0.75 mg/kg) it did not fully antagonize the effects of morphine.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are only reported for people and include abdominal pain and diarrhea. Although it is an opiate antagonist, it has not triggered breakthrough pain.

### Contraindications and Precautions

Do not use if there is intestinal obstruction.

### Drug Interactions

No drug interactions have been reported for animals.

## Instructions for Use

The use in animals is primarily experimental and has been limited in clinical practice.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Methylnaltrexone is available by injection only. It is available in 12-mg vials (0.6 mL), equivalent to 20 mg/mL in each vial.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- 0.15 mg/kg SQ injection once per 24 or 48 hours.

## Large Animal Dosage

### Horses

- 0.75 mg/kg IV q12h every 4 days.

## Regulatory Information

No withdrawal information is available for food-producing animals.

## Methylprednisolone

meth-il-pred-niss'oh-lone

**Trade and other names:** Methylprednisolone: Medrol; Methylprednisolone acetate: Depo-Medrol; and Methylprednisolone sodium succinate: Solu-Medrol

**Functional classification:** Corticosteroid

M

## Pharmacology and Mechanism of Action

Methylprednisolone is a glucocorticoid anti-inflammatory drug. Anti-inflammatory effects are complex, but they operate primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. Compared to prednisolone, methylprednisolone is 1.25 times more potent.

## Indications and Clinical Uses

Methylprednisolone acetate is a long-acting depot formulation of methylprednisolone. It is slowly absorbed from the IM injection site producing glucocorticoid effects for 3-4 weeks in some animals. Methylprednisolone acetate is used for intralesional therapy, intraarticular therapy, and inflammatory conditions. Methylprednisolone sodium succinate is a water-soluble formulation intended for acute therapy when high IV doses are needed for rapid effect. It is used for treatment of shock and CNS trauma. Methylprednisolone oral tablets are used for treatment of conditions in animals that require short-term to long-term therapy with an intermediate-acting corticosteroid. The indications for methylprednisolone tablets are similar to the use of prednisolone or prednisone tablets, except that methylprednisolone is slightly more potent. Conditions treated include dermatitis, immune-mediated diseases, intestinal diseases, and neurological and musculoskeletal diseases. Although high doses have been used to treat spinal cord trauma, this use has questionable benefit in animals. In large animals, methylprednisolone acetate is used for treatment of inflammatory conditions of the musculoskeletal system (intraarticular).



**Precautionary Information****Adverse Reactions and Side Effects**

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic–pituitary–adrenal (HPA) axis suppression. However, the manufacturer suggests that methylprednisolone causes less polyuria/polydipsia than prednisolone. Adverse effects include gastrointestinal ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Dogs that receive high doses of methylprednisolone succinate (e.g., 30 mg/kg) have a high risk of gastrointestinal bleeding. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs. Injections of methylprednisolone may activate latent feline herpes virus (FHV-1) infections in some cats. In cats, methylprednisolone acetate injections have caused injection-site alopecia. In horses, additional adverse effects may include risk of laminitis (although a direct link to induction of laminitis is controversial). In cats, methylprednisolone acetate administration causes volume expansion as a result of fluid shift secondary to hyperglycemia. This effect appears to increase risk of cats developing congestive heart failure (CHF) following methylprednisolone acetate administration.

**Contraindications and Precautions**

Use cautiously in patients prone to ulcers and infection or in animals in which wound healing is necessary. Use cautiously in diabetic animals, animals with kidney disease or pregnant animals. Use cautiously in cats because of volume expansion, especially cats at risk of CHF.

**Drug Interactions**

Like other corticosteroids, if methylprednisolone is administered with NSAIDs, there is increased risk of gastrointestinal ulcers.

**Instructions for Use**

Use of methylprednisolone is similar to other corticosteroids. Dose adjustment should be made to account for difference in potency. Use of methylprednisolone acetate should be evaluated carefully because one injection will cause glucocorticoid effects that persist for several days to weeks. Results of clinical studies in animals have not been reported for use of methylprednisolone sodium succinate.

**Patient Monitoring and Laboratory Tests**

Monitor liver enzymes, blood glucose, and kidney function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotrophic hormone stimulation test to monitor adrenal function. Monitor cats for diabetes and heart disease when treated with methylprednisolone acetate.

**Formulations**

- Methylprednisolone is available in 1-, 2-, 4-, 8-, 18-, and 32-mg tablets.
- Methylprednisolone acetate is available in 20- and 40-mg/mL suspension for injection.
- Methylprednisolone sodium succinate is available in 1- and 2-g and 125- and 500-mg vials for injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Methylprednisolone is insoluble in water and slightly soluble in ethanol. Methylprednisolone acetate is slightly soluble in water. Methylprednisolone sodium succinate is

highly soluble in water. When methylprednisolone sodium succinate is reconstituted, it should be used within 48 hours at room temperature. Decomposition occurs with longer storage. It may be frozen at  $-20^{\circ}\text{C}$  for 4 weeks with no loss of potency.

### Small Animal Dosage

#### Dogs

- Methylprednisolone: 0.22-0.44 mg/kg q12-24h PO.
- Methylprednisolone acetate: 1 mg/kg (or 20-40 mg/dog) IM q1-3wk.
- Methylprednisolone sodium succinate (for emergency use): 30 mg/kg IV and repeat at 15 mg/kg in 2-6 hours IV. Replacement or anti-inflammatory therapy: use 0.25-0.5 mg/kg/day.

#### Cats

- Methylprednisolone: 0.22-0.44 mg/kg q12-24h PO.
- Methylprednisolone acetate: 10-20 mg/cat IM q1-3wk.
- Methylprednisolone sodium succinate (for emergency use): 30 mg/kg IV and repeat at 15 mg/kg in 2-6 hours IV. Replacement or anti-inflammatory therapy: use 0.25-0.5 mg/kg/day.

### Large Animal Dosage

#### Horses

- 200 mg as a single total dose injected intramuscularly.
- Intraarticular dose: 40-240 mg total dose, with the average dose of 120 mg injected in the joint space using sterile technique.

### Regulatory Information

In horses, 200 mg per joint was detected in horses for 18 days. 100 mg per joint was detected for 7 days. For food animals, withdrawal times are not established. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Methyltestosterone

meth-ill-tess-toss'teh-rone

**Trade and other names:** Android and generic brands

**Functional classification:** Hormone, anabolic agent

### Pharmacology and Mechanism of Action

Anabolic androgenic agent. Injections of methyltestosterone will mimic effects of testosterone.

### Indications and Clinical Uses

Methyltestosterone is used for anabolic actions or testosterone hormone replacement therapy (androgenic deficiency). Testosterone has been used to stimulate erythropoiesis. Other similar agents used include testosterone cypionate and testosterone propionate.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects caused by excessive androgenic action of testosterone. Prostatic hyperplasia is possible in male dogs. Masculinization can occur in female dogs. Hepatopathy is more common with oral methylated testosterone formulations.

**Contraindications and Precautions**

Do not administer to pregnant animals.

**Drug Interactions**

No drug interactions have been reported for animals.

**Instructions for Use**

Use of testosterone androgens has not been evaluated in clinical studies in veterinary medicine. The clinical use is based primarily on experimental evidence or experiences in people.

**Patient Monitoring and Laboratory Tests**

Monitor hepatic enzymes and clinical signs for evidence of cholestasis and hepatotoxicity during treatment.

**Formulations**

- Methyltestosterone is available in 10- and 25-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- 5-25 mg/dog q24-48h PO.

**Cats**

- 2.5-5 mg/cat q24-48h PO.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

Do not use in animals intended for food.

Methyltestosterone is a Schedule III controlled drug.

RCI Classification: 4

**Metoclopramide Hydrochloride**

met-oh-kloe-prah'mide hye-droe-klor'ide

**Trade and other names:** Reglan and Maxolon

**Functional classification:** Antiemetic

**Pharmacology and Mechanism of Action**

Prokinetic drug. Antiemetic. Metoclopramide stimulates motility of the upper gastrointestinal tract and is a centrally acting antiemetic. The mechanism of action of metoclopramide is not completely understood. Among the proposed mechanisms is stimulation

of 5-HT<sub>4</sub> (serotonin) receptors or an increase in the release of acetylcholine in the gastrointestinal tract, possibly through a prejunctional mechanism. The affinity for 5-HT<sub>4</sub> receptors is low compared to other, more effective motility-modifying drugs. It inhibits gastric relaxation induced by dopamine, thus enhancing the cholinergic responses of gastric smooth muscle to increase motility. It also increases the tone of the lower esophageal sphincter. Metoclopramide acts centrally to inhibit dopamine in the CRTZ, which is responsible for antiemetic effects. The antiemetic effects are via its antidopamine (D<sub>2</sub>) action. The half-life in dogs has ranged from less than 1 hour to 2 hours; effects on esophageal sphincter persisted for only 30-60 minutes.

### Indications and Clinical Uses

Metoclopramide is used primarily for gastroparesis and treatment of vomiting. It is not effective for dogs with gastric dilation. In dogs, it is not very effective for decreasing gastroesophageal reflux or for increasing stomach emptying. The primary effect in dogs appears to be via its antiemetic properties (dopamine antagonism in the vomiting center). Because this drug transiently increases prolactin secretion, there has been interest in using it for treating agalactia in animals, but efficacy has not been determined. In horses, it has been used to treat intestinal postoperative ileus, but adverse effects have limited the use. It is not effective in ruminants. In people, metoclopramide has also been used to treat hiccups and lactation deficiency.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are primarily related to blockade of central dopaminergic receptors. Adverse effects similar to those that are reported for other centrally-acting D<sub>2</sub>-receptor antagonists such as phenothiazines. In horses, undesirable side effects have been common and limit the therapeutic use. Adverse effects in horses include behavioral changes, excitement, and abdominal discomfort. Excitement from IV infusions can be severe. In calves at doses >0.1 mg/kg, it produced neurologic effects.

#### Contraindications and Precautions

Do not use in patients with epilepsy or with diseases caused by gastrointestinal obstruction. Use cautiously in horses because dangerous behavior changes may occur. In people, it has been safe to use in the first trimester of pregnancy.

#### Drug Interactions

Efficacy is diminished when administered with parasympatholytic (atropine-like) drugs.

### Instructions for Use

Results of well-controlled clinical studies in animals have not been reported. Use in animals (and doses) is based primarily on studies in research animals, experience in people, or anecdotal experience in animals. Most use is for general antiemetic purposes, but doses as high as 2 mg/kg have been used to prevent vomiting during cancer chemotherapy (higher doses may produce antiserotonin effects). In horses, there is some increase in intestinal motility at recommended doses, but little effect on the large bowel has been seen. In calves, metoclopramide had little effect on rumen motility.

### Patient Monitoring and Laboratory Tests

Monitor for signs of behavior disturbances from treatment, especially when IV doses are administered.

**Formulations Available**

- Metoclopramide is available in 5- and 10-mg tablets, 1-mg/mL oral solution, and 5-mg/mL injection in 2-, 10-, and 30-mL vials.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. It is incompatible with other drugs when mixed in solution. Do not freeze. Stability is less than 24 hours if not protected from light. The solution has a pH of 4-5 and is stable over a pH range of 2-9. Individual doses may be stored in plastic syringes and are stable for 90 days in the refrigerator and 60 days at room temperature.

**Small Animal Dosage****Dogs and Cats**

- 0.2-0.5 mg/kg q6-8h IV, IM, or PO.
- CRI: Administer a loading dose of 0.4 mg/kg, followed by 0.3 mg/kg/hr. In refractory cases, CRI dose may be increased up to 1.0 mg/kg/hr. For antiemetic treatment with cancer chemotherapy, the dose used is up to 2 mg/kg per 24 hours.

**Large Animal Dosage****Horses**

- Infusion of metoclopramide (0.125-0.25 mg/kg/hr) added to IV fluids to reduce postoperative ileus in horses.

**Calves and Cattle**

- Not recommended because it is not a suitable prokinetic agent in ruminants. At a dose of 0.1 mg/kg IV to cattle, it does not increase abomasal emptying. Adverse reactions develop at higher doses (0.3 mg/kg).

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

**Metoprolol Tartrate**

meh-toe' proe-lole tar'trate

**Trade and other names:** Lopressor

**Functional classification:** Beta blocker

**Pharmacology and Mechanism of Action**

Beta<sub>1</sub>-adrenergic blocker. Metoprolol has similar properties to propranolol, except that metoprolol is specific for beta<sub>1</sub>-receptors, with less effect on beta<sub>2</sub>-receptors. Metoprolol is a lipophilic beta blocker and relies on the liver for clearance. Lipophilic beta blockers such as metoprolol undergo high first-pass clearance, which reduces oral bioavailability and causes high interpatient variability in plasma concentrations and effects. Alternative beta<sub>1</sub> blockers used in animals include atenolol.

## Indications and Clinical Uses

Metoprolol is used to control tachyarrhythmias and to control the response from adrenergic stimulation. Beta blockers effectively slow heart rate. Metoprolol is used in animals in which it is important to control ventricular rate, decrease conduction through the AV and SA nodes, and improve diastolic function. In animals, it has been used for tachyarrhythmias, hypertrophic cardiomyopathy, atrial fibrillation, and other cardiac diseases. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are primarily caused by excessive cardiovascular depression (decreased inotropic effects). Metoprolol may cause AV block.

#### Contraindications and Precautions

Use cautiously in animals prone to bronchoconstriction.

#### Drug Interactions

Lipophilic beta blockers such as metoprolol are subject to hepatic metabolism and may be prone to drug interactions that affect hepatic metabolizing enzymes. If administered with digoxin, it may potentiate an AV-nodal conduction block.

## Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

## Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during treatment.

## Formulations

- Metoprolol is available in 50- and 100-mg tablets and 1-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Metoprolol tartrate is soluble in water and ethanol. Protect tablets from moisture and freezing. Suspensions have been prepared in syrups and other flavorings with no loss of stability after 60 days of storage.

## Small Animal Dosage

### Dogs

- 5-50 mg/dog (0.5-1 mg/kg) q8h PO.

### Cats

- 2-15 mg/cat q8h PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Metronidazole, Metronidazole Benzoate

meh-troe-nye'dah-zole

**Trade and other names:** Flagyl and generic brands

**Functional classification:** Antibacterial, antiparasitic

### Pharmacology and Mechanism of Action

Antibacterial and antiprotozoal drug. It is a second-generation nitroimidazole in which the activity involves generation of free nitroradicals via metabolism within protozoa and bacteria. Metronidazole disrupts DNA in the organism via reaction with intracellular metabolite. Its action is specific for anaerobic bacteria and protozoa. Resistance is rare. It is active against some protozoa, including *Trichomonas*, *Giardia*, and intestinal protozoal parasites. It also has in vitro activity against anaerobic bacteria and *Helicobacter*. Metronidazole oral absorption is nearly complete in animals (75%-100% in horses and 60%-100% in dogs). Rectal absorption in horses is 30%. The half-life is 2-4 hours in horses, 9-12 hours in foals, and 4-5 hours in dogs. Metronidazole benzoate is formulated for cats to improve palatability. In this form, the oral absorption (12.4 mg/kg of the base) is 64%, with a half-life of 5 hours.

### Indications and Clinical Uses

Metronidazole is indicated to treat diarrhea and other intestinal problems caused by intestinal protozoa such as *Giardia*, *Trichomonas*, and *Entamoeba*. It may be used in small animals and horses for treatment of a variety of anaerobic infections. Common uses in horses include treatment of infections caused by *Clostridium* species, and *Bacteriodes fragilis*. Metronidazole has been used for immune-modulating activity in the intestine of animals and administered for inflammatory bowel disease in animals. However, evidence of a direct immune-modulating effect or immunosuppressive effect is lacking. Metronidazole benzoate, an ester pro-drug of metronidazole, has been used in cats because it is more palatable.

### Precautionary Information

#### Adverse Reactions and Side Effects

The most severe adverse effect is caused by toxicity to the CNS. High doses have caused lethargy, CNS depression, ataxia, tremors, seizures, vomiting, and weakness. Most CNS toxicity caused from metronidazole in animals occurs at high doses (>60 mg/kg/day). The CNS signs are related to inhibition of action of gamma aminobutyric acid (GABA) and are responsive to benzodiazepines (diazepam 0.4 mg/kg q8h for 3 days). In horses, adverse effects include peripheral neuropathy, hepatopathy, and decreased appetite, all of which are more likely with high doses. Foals have a longer half-life and may be more prone to adverse effects than adult horses. Like other nitroimidazoles, it has the potential to produce mutagenic changes in cells, but the clinical significance of this effect is uncertain. Like other nitroimidazoles, it has a bitter taste and can cause vomiting and anorexia. Metronidazole benzoate has been used in some cats safely at 25 mg/kg q12h for 7 days. However, there is a caution about the effect of benzoate salts in cats because it is a benzoic acid derivative. Benzoic acid can be toxic to cats and causes ataxia, blindness, respiratory problems, and other CNS disorders. Despite this concern, it is estimated that 500 mg/kg/day of metronidazole benzoate would be needed to provide a toxic dose of benzoic acid to cats. Nevertheless, any cat showing CNS or other signs of toxicity should have the metronidazole benzoate discontinued immediately.

### Contraindications and Precautions

Fetal abnormalities have not been demonstrated in animals with recommended doses, but use cautiously during pregnancy.

### Drug Interactions

Like other nitroimidazoles, it can potentiate the effects of warfarin and cyclosporine via inhibition of drug metabolism.

### Instructions for Use

Metronidazole is one of the most commonly used drugs for anaerobic infections. Although it is effective for giardiasis, other drugs used for *Giardia* include albendazole, fenbendazole, and quinacrine. Central nervous system toxicity is a concern, but it is dose related. The maximum dose that should be administered is 50-65 mg/kg per day in any species. Metronidazole is unpalatable and can produce a metallic taste. In cats, when the tablet is crushed or broken, the unpalatability is particularly a problem. Metronidazole benzoate has a bland taste and is better tolerated. Metronidazole benzoate is not commercially available in the US. However, it may be available from compounding pharmacies. Because of the weight of metronidazole benzoate versus metronidazole hydrochloride, a factor of 1.6 times is used to convert a metronidazole hydrochloride dose to a metronidazole benzoate dose. Metronidazole benzoate is 62% metronidazole; therefore 20 mg/kg of metronidazole benzoate delivers 12.4 mg/kg of metronidazole.

In horses, oral absorption of metronidazole is practically complete and not affected by feeding pattern (e.g., with or without food, and similar with hay or concentrate). However, absorption from rectal administration to horses is low.

Metronidazole should not be injected directly; it is too acidic. See “[Stability and Storage](#)” section for mixing instructions.

### Patient Monitoring and Laboratory Tests

Monitor for neurologic adverse effects. Minimum inhibitory concentrations (MIC) for anaerobic bacteria are typically 2-4 mcg/mL, or less. The CLSI breakpoint is less than, or equal to 8 mcg/mL.

### Formulations

- Metronidazole is available in 250- and 500-mg tablets, 375-mg capsules, 50-mg/mL suspension, and 5-mg/mL injection.
- Metronidazole benzoate is a formulation not available in the US but has been compounded for veterinary use. Metronidazole benzoate is 62% metronidazole. It has been formulated in Oral-Plus and Ora-Sweet (drug excipients) to a concentration of 16 mg/mL.

### Stability and Storage

The base is slightly soluble in water. The benzoate form is practically insoluble; the hydrochloride form is soluble in water. Metronidazole has been crushed and mixed with some flavorings to mask the taste. When mixed with some syrups or water, with exceptions listed here, decomposition occurs within 28 days. Metronidazole benzoate prepared in vehicles such as Ora-Plus or Ora-Sweet was stable for 90 days. Metronidazole base (from tablets) also was mixed with these vehicles and was found to be stable for 90 days.

When reconstituted, metronidazole hydrochloride is too acidic (pH 0.5-2) for direct injection. Injection of 5 mg/mL should be further diluted with 100 mL (0.9% saline, 5% dextrose, or Ringer's solution) and neutralized with 5 mEq sodium bicarbonate per 500 mg for a pH of 6-7. Reconstituted injectable forms are stable for 96 hours but after dilution should be discarded after 24 hours.



## Small Animal Dosage

### Dogs

- Anaerobes: 15 mg/kg q12h or 12 mg/kg q8h PO.
- Anaerobes: IV dose: 15 mg/kg IV via slow infusion in a diluted form.
- *Giardia*: 12-15 mg/kg q12h for 8 days PO.

### Cats

- Anaerobes: 10-25 mg/kg q24h PO.
- *Giardia*: 17 mg/kg (one third tablet per cat) q24h for 8 days.
- Metronidazole benzoate (for treatment of *Giardia*): 25 mg/kg PO 12h for 7 days. Metronidazole benzoate is 62% metronidazole; therefore 20 mg/kg of metronidazole benzoate delivers 12.4 mg/kg metronidazole.

## Large Animal Dosage

### Horses

- Treatment of anaerobic and protozoal infections: 10 mg/kg q12h PO. Note: Some clinicians have used higher doses (up to 15-20 mg/kg q6h), but at these doses, side effects are more likely.
- Foals: 10-15 mg/kg IV or PO q12h.

### Cattle

- Treatment of trichomoniasis (bulls): 75 mg/kg q12h IV for three doses.

## Regulatory Information

Do not administer to animals that produce food. Administration of nitroimidazoles to animals intended for food is prohibited. Treated cattle must not be slaughtered for food.

## Mexiletine

meks-il'eh-teen

**Trade and other names:** Mexitil

**Functional classification:** Antiarrhythmic

## Pharmacology and Mechanism of Action

Antiarrhythmic drug. Mexiletine is a Class IB antiarrhythmic agent. Mechanism of action is to block the fast sodium channel and depress Phase 0 of depolarization. Because lidocaine is not absorbed orally, mexiletine has been used when oral administration is needed in dogs. It has a similar mechanism of action as lidocaine. It is absorbed approximately 90% in people without significant first-pass effects. It is presumed to have good absorption also in dogs, although this has not been studied.

An additional use of mexiletine is for treating chronic pain. It is used to treat pain caused by diabetic neuropathy and nerve injury at lower doses than the antiarrhythmic dose.

## Indications and Clinical Uses

Mexiletine has been used to treat ventricular arrhythmias. Although lidocaine is often the first Class I antiarrhythmic agent used for injection in the hospital, when longer-term treatment with an oral drug is needed, mexiletine is often the first choice.

The doses used in dogs are derived from empirical use and extrapolation from human medicine. It is often used in combination with sotalol or atenolol (Class II

and Class III antiarrhythmic agents, respectively) because it may have better electrophysiological effects when used in combination. It may also counteract the adverse effects of sotalol on the action potential duration.

### Precautionary Information

#### Adverse Reactions and Side Effects

In dogs, the most common adverse effects are gastrointestinal problems. High doses may cause excitement and tremors. Mexiletine can be arrhythmogenic in some animals. In people, related drugs (flecainide and encainide) can be proarrhythmogenic and associated with excessive mortality.

#### Contraindications and Precautions

Use cautiously in animals with liver disease.

#### Drug Interactions

Sotalol will increase plasma drug concentrations.

### Instructions for Use

Results of controlled clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people, research studies in experimental dogs, or anecdotal experience in animals. Administer with food to decrease gastrointestinal problems.

### Patient Monitoring and Laboratory Tests

Monitor ECG during use. Effective plasma drug concentrations are 0.75-2.0 mcg/mL (extrapolated from people).

### Formulations

- Mexiletine is available in 150-, 200-, and 250-mg capsules.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is freely soluble in water and ethanol.

### Small Animal Dosage

#### Dogs

- 6-10 mg/kg q8-12h PO.
- Chronic pain caused by nerve injury: 4-10 mg/kg PO q8h.

#### Cats

No safe dose has been established.

### Large Animal Dosage

- No large animal doses have been reported.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 4

## Mibolerone

mih-bole'er-one

**Trade and other names:** Cheque Drops

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Androgenic steroid. Mibolerone will mimic androgens in the body.

### Indications and Clinical Uses

Mibolerone is used to suppress estrus in animals. The primary indication is to prevent estrus in adult female dogs.

### Precautionary Information

#### Adverse Reactions and Side Effects

Many bitches show clitoral enlargement or discharge from treatment.

#### Contraindications and Precautions

Do not use in Bedlington terriers. Do not administer to pregnant animals. Do not use with perianal adenoma or carcinoma. Do not use in cats. Mibolerone has been abused in people for use as a body-building drug. Therefore extreme caution should be used when dispensing this medication to animal owners.

#### Drug Interactions

No drug interactions have been reported.

### Instructions for Use

Treatment ordinarily is initiated 30 days prior to onset of estrus. Continue treatment as long as needed, but it is not recommended to be used for more than 2 years. Mibolerone should not be used in bitches before the first estrous period. It is not intended for animals being used primarily for breeding purposes.

### Patient Monitoring and Laboratory Tests

Monitor hepatic enzymes periodically if used chronically.

### Formulations

- Mibolerone has been discontinued by the manufacturer. However, it may be available from some other sources. Originally, it was available in 100-mcg/mL oral solution.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 2.6-5 mcg/kg/day PO.
- Bitches weighing 0.45-11.3 kg: 30 mcg/day PO.
- Bitches weighing 11.8-22.7 kg: 60 mcg/day PO.
- Bitches weighing 23-45.3 kg: 120 mcg/day PO.
- Bitches weighing more than 45.8 kg: 180 mcg/day PO.

#### Cats

- Safe dose not established.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Do not administer to animals that produce food.

## Midazolam Hydrochloride

mid'az'oe-lam hye-droe-klor'idē

**Trade and other names:** Versed

**Functional classification:** Anticonvulsant, Sedative

## Pharmacology and Mechanism of Action

Benzodiazepine. Central-acting CNS depressant. Midazolam, like other benzodiazepines, binds to a specific GABA-binding site. It may modify the GABA-binding sites and increase the action of GABA on nerve cells. Sedative effects of midazolam may be attributed to potentiation of GABA pathways that act to regulate release of monoamine neurotransmitters in the CNS. Benzodiazepines may act as muscle relaxants by inhibiting certain spinal pathways or directly depressing motor nerve and muscle function. Pharmacokinetics have been studied in dogs and horses. In dogs, the half-life is variable (1-2 hours) with a high clearance (10-27 mL/kg/min). Oral absorption in dogs is variable from IM administration (50%-90%), but negligible from rectal administration. Metabolites are negligible in dogs. Peak plasma concentrations in dogs from IM injection is 7-8 minutes. In horses, the terminal half-life is 2-5.8 hours at 0.05 mg/kg IV and 3.2-15 hours at 0.1 mg/kg IV. Clearance in horses is approximately 10 mL/kg/minute.

## Indications and Clinical Uses

Midazolam is used as an anesthetic adjunct, frequently with other anesthetics. It is used for similar indications as diazepam, but because it is water soluble, midazolam can be administered in an aqueous vehicle and administered intramuscularly compared to other drugs of this class (drugs such as diazepam are not water soluble). It has been mixed with other water-soluble anesthetic agents in the same syringe (e.g., ketamine and  $\alpha_2$  agonists) and administered intravenously. In horses, it has been administered in the same solution with ketamine and xylazine.

In animals, it also has been administered as an anticonvulsant, muscle relaxant, and sedative. In foals, it has been used to treat neonatal seizures (see dose protocols).

## Precautionary Information

### Adverse Reactions and Side Effects

Midazolam administered intravenously can cause serious cardiorespiratory depression. Some animals may experience paradoxical excitement. Chronic administration may lead to dependence and a withdrawal syndrome if discontinued. In horses, it causes ataxia, swaying, agitation, and weakness shortly after IV administration. If severe adverse reactions occur, consider administering an antagonist (flumazenil, Romazicon).

### Contraindications and Precautions

Use cautiously when administered intravenously, especially with opiates.

### **Drug Interactions**

Compared to diazepam, it is water soluble and is more compatible with fluid solutions. It has been administered safely with several anesthetics, sedatives, preanesthetics, and anticonvulsants. However, midazolam is metabolized in the liver by P450 enzymes which may be inhibited by some drugs (see Appendix I). For example ketoconazole will inhibit clearance of midazolam in dogs.

### **Instructions for Use**

Clinical trials have not been reported, although use of midazolam is reported in some anesthetic protocols for animals. Unlike other benzodiazepines, midazolam can be administered intramuscularly.

### **Patient Monitoring and Laboratory Tests**

Samples of plasma or serum may be analyzed for concentrations of benzodiazepines. Plasma concentrations in the range of 100-250 ng/mL have been cited as the therapeutic range for people. Other references have cited this range as 150-300 ng/mL. However, there are no readily available tests for monitoring in many veterinary laboratories. Laboratories that analyze human samples may have nonspecific tests for benzodiazepines. With these assays, there may be cross-reactivity among benzodiazepine metabolites.

### **Formulations**

- Midazolam is available in 5-mg/mL injection.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Solubility of midazolam in water is pH dependent. At lower pH values (pH <4), it becomes more soluble. It can be mixed for short-term use with other water-soluble anesthetics if administered immediately after mixing. Midazolam and ketamine hydrochloride are compatible when mixed in the same syringe.

### **Small Animal Dosage**

#### **Dogs**

- 0.1-0.25 mg/kg IV or IM.
- 0.1-0.3 mg/kg/hr IV infusion.
- Status epilepticus: 0.1-0.2 mg/kg IV bolus.

#### **Cats**

- Sedation: 0.05 mg/kg IV.
- Induction of anesthesia: 0.3-0.6 mg/kg IV combined with 3 mg/kg ketamine. (Additional doses of ketamine at 1-2 mg/kg can be administered as needed.)

### **Large Animal Dosage**

#### **Pigs**

- Up to 0.5 mg/kg IM, usually in combination with ketamine.

#### **Horses**

- Neonatal seizures in foals: 0.1-0.2 mg/kg (5-10 mg per foal) IV, over 15-20 min or IM, followed by 3 mg/hr IV (range of 2-6 mL/hr) CRI to control seizures. Infusion dose is prepared by adding 10 mL (5 mg/mL) to 100 mL saline to make a solution of 0.5 mg/mL.
- Anesthetic adjunct in horses: 0.1 mg/kg IV, administered with ketamine (2.2 mg/kg) or other anesthetics (e.g., xylazine).

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).  
Schedule IV controlled drug  
RCI Classification: 2

## Milbemycin Oxime

mil-beh-mye'sin ahk'seem

**Trade and other names:** Interceptor, Interceptor Flavor Tabs, and Safeheart

Milbemycin also is an ingredient in Sentinel. It is combined with spinosad in Trifexis.

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Antiparasitic drug. Avermectins (ivermectin-like drugs) and milbemycins (milbemycin and moxidectin) are macrocyclic lactones and share similarities, including mechanism of action. These drugs are neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Paralysis and death of the parasite are caused by increased permeability to chloride ions and hyperpolarization of nerve cells. These drugs also potentiate other chloride channels, including ones gated by GABA. Mammals ordinarily are not affected because they lack glutamate-gated chloride channels, and there is a lower affinity for other mammalian chloride channels. Because these drugs ordinarily do not penetrate the blood-brain barrier, GABA-gated channels in the CNS of mammals are not affected. Milbemycin is active against intestinal parasites, mites, bots, heartworm microfilaria, and developing larvae. Milbemycin has no effect on trematode or cestode parasites.

## Indications and Clinical Uses

Milbemycin is used as a heartworm preventative, miticide, and microfilaricide. It is also used to control infections of hookworm, roundworms, and whipworms. It has been used in combination with flea control drugs (see Sentinel, which contains milbemycin oxime and lufenuron). At high doses, it has been used to treat *Demodex* infections in dogs (see [dosing](#) section).

## Precautionary Information

### Adverse Reactions and Side Effects

At doses of 5 mg/kg, it was well tolerated in most dogs (10 times the heartworm dose). At 10 mg/kg (20 times the heartworm dose), it caused depression, ataxia, and salivation in some dogs. Toxicity may occur at high doses and in breeds in which milbemycin crosses the blood-brain barrier at doses as low as 1.5 mg/kg per day. Sensitive breeds include collies, Australian shepherds, Old English sheepdogs, longhaired whippets, and Shetland sheepdogs. Toxicity is neurotoxic, and signs include depression, ataxia, difficulty with vision, coma, and death. Sensitivity to milbemycin occurs in certain breeds because of a mutation in the multidrug resistance gene (ABCB1 gene) that codes for the membrane pump P-glycoprotein. This mutation affects the efflux pump in the blood-brain barrier. Therefore milbemycin can accumulate in the brains of susceptible animals. High doses in normal animals may also produce similar toxicosis. However, at doses used for

heartworm prevention, this effect is unlikely. At high doses used for treating *Demodex* infections, diarrhea may occur in some dogs.

### **Contraindications and Precautions**

Do not use in dogs that have shown sensitivity to ivermectin or other drugs in this class (see previous breed list). Treatment using three times the daily doses from mating to 1 week before weaning did not produce any adverse effects in the pregnant bitch, the fetus, or puppies. One-time doses of three times the monthly rate before or shortly after whelping caused no adverse effects on the puppies. Milbemycin is excreted in milk. Puppies given milbemycin at 19 times the regular dose showed adverse effects, but signs were transient for only 24-48 hours.

In cats, it is generally well tolerated. In cats treated for *Demodex* at high doses (1-2 mg/kg), some vomiting and diarrhea can be observed, but neurologic signs are rare.

### **Drug Interactions**

Do not use with drugs that may increase penetration across the blood-brain barrier. Such drugs include p-glycoprotein inhibitors such as ketoconazole, cyclosporine, quinidine, and some macrolide antibiotics (see Appendix J for list of p-glycoprotein inhibitors).

## **Instructions for Use**

Doses vary depending on parasite treated. Treatment of demodicosis requires a higher dose administered daily than the heartworm preventative dose. For *Demodex*, use a protocol of 1 mg/kg/day until clinical cure followed by 3 mg/kg/week for a parasitological cure. Treatment can be long because it may require 4 months for a clinical cure and 8 months for a parasitological cure.

## **Patient Monitoring and Laboratory Tests**

Monitor for heartworm status in dogs before initiating treatment with milbemycin.

## **Formulations Available**

- Milbemycin is available in 2.3-, 5.75-, 11.5-, and 23-mg tablets. It is also found in other combination products (e.g., with spinosad in Trifexis).

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## **Small Animal Dosage**

### **Dogs**

- Heartworm prevention and control of endoparasites: 0.5 mg/kg q30days PO.
- Demodicosis: 2 mg/kg q24h PO for 60-120 days or 1 mg/kg daily until a clinical cure is observed, followed by 3 mg/kg once per week until a parasitological cure (negative scraping) is observed.
- Sarcoptic mange: 2 mg/kg q7days for 3-5 weeks PO.
- Cheyletiellosis: 2 mg/kg/wk PO.

### **Cats**

- Heartworm and endoparasite control: 2 mg/kg q30days PO.
- Demodicosis in cats: 1-2 mg/kg q24h, PO.

## **Large Animal Dosage**

- No large animal doses have been reported.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Mineral Oil

**Trade and other names:** Generic brands

**Functional classification:** Laxative

## Pharmacology and Mechanism of Action

Lubricant laxative. Mineral oil increases water content of stool and acts as a lubricant for intestinal contents.

## Indications and Clinical Uses

Mineral oil is administered orally (via stomach tube in horses) to increase passage of feces for treatment of impaction and constipation.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects have not been reported. Chronic use may decrease absorption of fat-soluble vitamins.

### Contraindications and Precautions

Use caution when administering via stomach tube. Accidental administration into the lungs has produced fatal reactions.

### Drug Interactions

No drug interactions reported. Chronic use may inhibit absorption of fat-soluble vitamins.

## Instructions for Use

Use is empirical. No clinical results reported.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Mineral oil is available in an oral liquid.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 10-50 mL/dog q12h PO.

### Cats

- 10-25 mL/cat q12h PO.

## Large Animal Dosage

### Horses and Cattle

- 500-1000 mL (1 pint to 1 quart) per horse or cow PO as needed. Up to 2-4 L per adult horse or cow PO (usually administered via stomach tube).



**Sheep and Pigs**

- 500-1000 mL PO as needed.

**Regulatory Information**

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

**Minocycline Hydrochloride**

min-oh-sye'kleen hye-droe-klor'idē

**Trade and other names:** Minocin, Solodyn

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Tetracycline antibiotic. Like other tetracyclines, the mechanism of action of minocycline is to bind to 30S ribosomal subunits and inhibit protein synthesis. It is usually bacteriostatic. It has a broad spectrum of activity, including gram-positive and gram-negative bacteria, some protozoa, *Rickettsiae*, and *Ehrlichiae*. Resistance among *Staphylococcus* species and gram-negative bacilli may be common, but some methicillin-resistant *Staphylococcus* spp. may be susceptible to minocycline that are not susceptible to doxycycline. Resistance is mediated by genes called *tet* genes. For example, *tet(M)* prevents binding of tetracyclines to ribosomes and confers resistance to all tetracyclines. The *tet(K)* mediates resistance by preventing entry into bacteria and confers resistance to other tetracyclines, but not minocycline.

Minocycline also may have some anti-inflammatory properties that may benefit joint diseases. It has a similar pharmacokinetic profile to doxycycline, but less protein binding. In horses, oral minocycline at 4 mg/kg every 12 hours produced a peak concentration of 0.6 mcg/mL and had a half-life of approximately 13 hours; after IV administration at 2.2 mg/kg, the half-life is 7.7 hours. The half-life in dogs and cats after an oral dose is 4.1 and 6.3 hours, respectively. The oral absorption is 50% and 63% in dogs and cats, respectively.

**Indications and Clinical Uses**

Minocycline is used when tetracyclines are indicated for treating bacterial infections in animals. It may be effective for *Rickettsiae* and *Ehrlichiae* infections. The clinical use is similar to doxycycline. It may be substituted for doxycycline to treat heartworm-positive dogs because of its activity against *Wolbachia*.

**Precautionary Information****Adverse Reactions and Side Effects**

The most common adverse effect from administration of minocycline has been gastrointestinal problems, primarily vomiting and nausea. The gastrointestinal effects are more likely as the dose is increased. Otherwise, it has been used safely in experimental animals without adverse effects. As with any oral tetracycline, changes in intestinal microflora could increase risk of diarrhea in some animals. Rapid IV injection has been associated with adverse events in people, but when administered intravenously to dogs, horses, and cats, no adverse events were observed.

**Contraindications and Precautions**

No specific precautions have been reported for animals.

### Drug Interactions

No drug interactions are reported for animals. Oral absorption may be affected by oral products that contain cations, such as calcium, aluminum, iron, and magnesium.

### Instructions for Use

Because of shortages of other tetracyclines or high expense of doxycycline, minocycline has received increased attention for treating dogs, cats, and horses. In dogs, oral absorption is higher when administered without food. If possible, administer minocycline at least 30 minutes prior to a meal in dogs.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for susceptible organisms are  $\leq 0.5$  mcg/mL. Tetracycline has been used as a marker to test susceptibility for other drugs in this class such as doxycycline, minocycline, and oxytetracycline. If an isolate is susceptible to tetracycline, it is also susceptible to minocycline.

### Formulations

- Minocycline is available in 50-, 75-, and 100-mg tablets and capsules and 10-mg/mL flavored oral suspension. Vials for injection should be reconstituted in 5 mL and then diluted in 500-1000 mL for IV infusion. Solution may be stored at room temperature for 24 hours.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with other drugs.

### Small Animal Dosage

#### Dogs

- 5 mg/kg q12h PO will be sufficient in most dogs. For higher MIC values, administer 10 mg/kg twice daily, but the higher dose is more likely to produce vomiting.
- If IV administration is used, reduce dose by one-half compared to the oral dose.

#### Cats

- 8.8 mg/kg (or 50 mg per cat) PO once daily.

### Large Animal Dosage

#### Horses

- 4 mg/kg q12h PO, or 2.2 mg/kg q12h IV.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Mirtazapine

Mir taz' a peen

**Trade and other names:** Remeron

**Functional classification:** Antiemetic agent

## Pharmacology and Mechanism of Action

Mirtazapine is used as an antiemetic in animals, but in people, it also has antidepressant and anxiolytic activity. The most common use in cats is as an appetite stimulant rather than as an antiemetic. The antiemetic action is via blockade of serotonin (5HT<sub>3</sub>, 5HT<sub>2</sub>, and 5HT<sub>1</sub>) receptors and antagonism of alpha<sub>2</sub>-receptors. Because it is active on three serotonin receptors, it is not as selective as ondansetron and other related drugs that affect 5HT<sub>3</sub> receptors. Presynaptic alpha<sub>2</sub> antagonism increases noradrenergic and serotonergic transmission. Serotonin 5HT<sub>2</sub> and 5HT<sub>3</sub> receptors are blocked postsynaptically. Appetite stimulant effects are most likely via the 5-HT<sub>3</sub> antagonist properties. After administration to cats, the half-life was 15 hours after a high dose (3.75 mg per cat) and 9-10 hours after a low dose (1.9 mg per cat). The half-life is longer (15 hours) in cats with chronic kidney disease, necessitating a less frequent dosing interval in these cats (see [dosing](#) section).

## Indications and Clinical Uses

Mirtazapine is used as an antiemetic and appetite stimulant, primarily in cats. Although there also has been some use in dogs, it is primarily anecdotal. After introduction of other antiemetics for animals (e.g., maropitant), the use of mirtazapine has declined. In cats, mirtazapine administered at 1.9 mg per cat every 48 hours for 3 weeks increased appetite, activity, and weight in cats with kidney disease.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects observed in cats include twitching and other abnormal behavior. Although this drug acts through serotonergic mechanisms, risk of development of serotonin syndrome is low. At high doses to cats, ataxia, restlessness, vomiting, vocalization, and cardiovascular effects have been observed. In people, sedation and weight gain have been reported. Some antihistaminic effects have been reported, but sedation observed in people has not been as common in animals. Cyproheptadine (a serotonin antagonist) can be considered an antagonist in the event of overdose or adverse effects.

#### Contraindications and Precautions

No known contraindications in animals.

#### Drug Interactions

No drug interactions have been reported for animals. However, avoid use with selective serotonin reuptake inhibitors (SSRIs) and MAOIs such as selegiline.

## Instructions for Use

Doses and recommendations are based primarily on the clinical use in cats with chronic kidney disease. Other uses are anecdotal and not well documented.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Mirtazapine is available in 15-, 30-, and 45-mg tablets. There is also a rapidly disintegrating tablet in these sizes that dissolves easily in a pet's mouth.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 0.5 mg/kg q24h PO. Generally in the range of 3.75-7.5 mg per dog daily PO.

### Cats

- 1.9 mg per cat PO. Doses have ranged from 3.75-7.5 mg per cat, per day, PO (one fourth to one half of a 15-mg tablet). In healthy cats, it can be administered once daily. In cats with chronic kidney disease, increase interval to q48h.

## Large Animal Dosage

No large animal doses are available.

## Regulatory Information

No withdrawal time information is available for food-producing animals.

## Misoprostol

mee-soe-pross'tole

**Trade and other names:** Cytotec

**Functional classification:** Antiulcer agent

## Pharmacology and Mechanism of Action

Misoprostol is a synthetic prostaglandin. It is a synthetic analogue of prostaglandin E<sub>1</sub> (PGE<sub>1</sub>) and produces a cytoprotective effect on the gastrointestinal mucosa. It has been shown in dogs and people to decrease injury to gastrointestinal mucosa caused by NSAIDs, such as aspirin. In studies in dogs, misoprostol was not effective for decreasing adverse effects caused by corticosteroids. Misoprostol also has anti-inflammatory effects and has been used to treat pruritus in dogs.

## Indications and Clinical Uses

Misoprostol is used to decrease the risk of gastrointestinal ulceration when administered concurrently with NSAIDs. Efficacy has been established for this indication in trials with aspirin but not with other NSAIDs in animals. There is no evidence to show that it decreases gastrointestinal bleeding caused from other drugs (e.g., corticosteroids). Clinical trials also are available to show that misoprostol is effective for treating pruritus in patients with atopic dermatitis, although it is less effective than other drugs.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are caused by effects of prostaglandins. Most common adverse effects are gastrointestinal discomfort, vomiting, and diarrhea.

### Contraindications and Precautions

Do not administer to pregnant animals; it may cause abortion. Women should handle this medication carefully because it can induce abortion.

### Drug Interactions

No drug interactions reported for animals.

## Instructions for Use

Doses and recommendations are based on clinical trials in which misoprostol was administered to prevent gastrointestinal mucosal injury caused by aspirin.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Misoprostol is available in 0.1-mg (100 mcg) and 0.2-mg (200-mcg) tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 2-5 mcg/kg q12h PO.
- Atopic dermatitis: 5 mcg/kg q8h PO.

### Cats

- Dose has not been established.

## Large Animal Dosage

### Horses

- 5 mcg/kg q8h PO. However, there may be unacceptable gastrointestinal adverse effects in large animals.

## Regulatory Information

Do not use in animals that produce food.

RCI Classification: 4

## Mitotane

mye'toe-tane

**Trade and other names:** Lysodren and op'-DDD

**Functional classification:** Adrenolytic agent

## Pharmacology and Mechanism of Action

Mitotane is a cytotoxic agent. It binds to adrenal proteins and is then converted to a reactive metabolite, which then destroys cells of the zona fasciculata and zona reticularis of the adrenal cortex. Destruction of the adrenal cells is relatively specific and can be complete or partial, depending on the dose used. If only partial destruction of adrenal cortical cells occurs, repeated administration or maintenance doses are needed to suppress hypercortisolemia.

Mitotane is a highly lipophilic drug. It is poorly absorbed without food, but oral absorption is enhanced when administered with food or oil.

## Indications and Clinical Uses

Mitotane is used primarily to treat pituitary-dependent hyperadrenocorticism (PDH) (Cushing disease). It also has been used to treat adrenal tumors. Treatment is initiated with a loading dose, followed by weekly maintenance doses. Other drugs used to suppress cortisol in dogs include ketoconazole, selegiline, and trilostane. Treatment with mitotane has been compared with trilostane and has shown that each drug,

although acting through different mechanisms, produces similar survival times in dogs with PDH.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects, especially during the induction period, include lethargy, weakness, anorexia, ataxia, depression, and vomiting. Discontinue if signs of liver disease are observed. Adverse effects may occur in 25%-30% of dogs. Corticosteroid supplementation (e.g., hydrocortisone or prednisolone) may be administered to minimize side effects (prednisone dose 0.25 mg/kg/day). Aldosterone secretion may be reduced in some dogs after treatment.

In some dogs, adverse neurologic signs may be observed, which include ataxia, head pressing, and blindness. Central nervous system effects are the result of enlargement of the pituitary gland in response to suppression of the adrenal cortex and lack of feedback by cortisol. Loss of feedback control stimulates corticotropin-releasing hormone (CRH) and adrenocorticotrophic hormone (ACTH) secretion.

#### Contraindications and Precautions

Do not administer to animals unless there is an ability to monitor response with cortisol serum measurements, preferably after ACTH stimulation.

#### Drug Interactions

No drug interactions are reported for animals.

### Instructions for Use

Dose and frequency are often based on patient response. Typically, the induction period lasts 5-14 days in dogs. During the induction period, monitor water consumption, appetite, and behavior. Adverse effects are common during initial therapy. Administration with food increases oral absorption. The maintenance dose should be adjusted on the basis of periodic cortisol measurements and ACTH stimulation tests. Prednisolone at 0.25 mg/kg is sometimes administered as a replacement in patients with PDH during the induction treatment. Trilostane, an approved drug for dogs, has also been used instead of mitotane in dogs and should be considered when dogs do not respond to or tolerate mitotane. Cats usually have not responded to mitotane treatment.

### Patient Monitoring and Laboratory Tests

Monitor water consumption and appetite during the induction phase. Monitor ACTH response test to adjust dose. Monitor electrolytes periodically to screen for hyperkalemia that could result from adrenal destruction (iatrogenic hypoadrenocorticism).

### Formulations

- Mitotane is available in 500-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Mitotane is not stable in aqueous solutions and may lose potency in some compounded formulations.

### Small Animal Dosage

#### Dogs

- PDH: 50 mg/kg/day (in divided doses) PO for 5-14 days, then 50-70 mg/kg/week PO.
- Adrenal tumor: 50-75 mg/kg/day for 10 days, then 75-100 mg/kg/week PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Do not use in animals that produce food.

## Mitoxantrone Hydrochloride

mye-toe-zan'trone hye-droe-klor'ide

**Trade and other names:** Novantrone

**Functional classification:** Anticancer agent

## Pharmacology and Mechanism of Action

Anticancer antibiotic. Mitoxantrone is an anticancer agent that is similar to doxorubicin in action. Like doxorubicin, it acts to intercalate between bases on DNA, disrupting DNA and RNA synthesis in tumor cells. Mitoxantrone may affect tumor cell membranes.

## Indications and Clinical Uses

Mitoxantrone is used in anticancer drug protocols in animals for treatment of leukemia, lymphoma, and carcinomas.

## Precautionary Information

### Adverse Reactions and Side Effects

As with all anticancer agents, certain adverse effects are predictable and unavoidable and related to the drug's action. Mitoxantrone produces myelosuppression, vomiting, anorexia, and gastrointestinal upset, but it may be less cardiotoxic than doxorubicin.

### Contraindications and Precautions

Do not administer to animals with bone marrow suppression.

### Drug Interactions

No drug interactions are reported for animals.

## Instructions for Use

Proper use of mitoxantrone usually follows a specific anticancer protocol. Doses listed are based on input from reputable oncologists, but consult specific protocol for dosing regimens that may deviate from these recommendations.

## Patient Monitoring and Laboratory Tests

Monitor CBC to look for evidence of bone marrow toxicity.

## Formulations

- Mitoxantrone is available in 2-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 5-5.5 mg/m<sup>2</sup> IV every 21 days, and up to 6 mg/m<sup>2</sup> if dogs tolerate it well.

**Cats**

- 6-6.5 mg/m<sup>2</sup> IV every 21 days.

**Large Animal Dosage**

- No large animal doses have been reported.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

**Mitratapide**

Mi-trat'-a-pyed

**Trade and other names:** Yarvitan

**Functional classification:** Weight loss medication

**Pharmacology and Mechanism of Action**

Mitratapide is used to produce weight loss in dogs. It is related to another medication used for obesity in dogs: dirlotapide (Slentrol). Mitratapide is an inhibitor of the microsomal triglyceride transfer protein (MTP). Inhibition of this enzyme reduces the ability of intestinal enterocytes to process triglycerides. The accumulation of these triglycerides in the intestinal cells sends a signal to the CNS to suppress the appetite. In dogs, the effect on the intestinal cells reduces the uptake of dietary lipids in association with decreased postprandial serum triglycerides, phospholipids, and cholesterol. The accumulation of triglycerides inside the enterocytes can be observed macroscopically and histopathologically. The weight loss is attributed to the reduced appetite, rather than impaired processing of dietary lipids. It does not produce a direct centrally acting effect. Bioavailability of oral mitratapide is 16%-21%, with a large volume of distribution (VD) of 5 liters/kg. It is highly protein bound (99%). It has a plasma half-life of 6.3 hours for mitratapide and longer (9.8, 11.7, 44.7 hours) for various metabolites, some of which are active.

**Indications and Clinical Uses**

Mitratapide is used in the management of obesity in dogs. During the treatment protocol, there is a relatively moderate loss of weight, (6%-7% of the weight before treatment). It should not be used without instituting the proper protocol as outlined by the sponsor. It should be used in an overall weight management program, which also includes appropriate dietary changes. Before using to treat overweight or obesity, rule out other diseases such as hypothyroidism or hyperadrenocorticism. At this time, it is approved in Europe, but it has not been approved in the US. It should not be used in cats.

**Precautionary Information****Adverse Reactions and Side Effects**

Decreased appetite occurs as a mode of action of the drug. Vomiting may also occur as a common effect related to the drug's mechanism of action. Nausea and diarrhea also may occur. None of these signs are necessarily cause to stop the medication, and they may resolve with time. However, if vomiting and nausea persist, evaluation and adjustment of dose may be necessary. Administration with food may decrease vomiting. Changes in liver enzymes also are expected. There



may be decreases in serum albumin, globulin, total protein, calcium, and alkaline phosphatase and increases in alanine aminotransferase (ALT) associated with treatment. Hyperkalemia may also be observed. The severity of these changes is proportional to dose. These changes may normalize after continued treatment. There may be decreased absorption of fat-soluble vitamins A and E. The reduced absorption of these vitamins has not been clinically significant.

### **Contraindications and Precautions**

Do not administer to cats. Do not use in dogs with liver disease. Do not use in dogs during pregnancy and lactation or in young dogs less than 18 months of age. Humans should not take this drug.

### **Drug Interactions**

No drug interactions have been reported. It has been safely administered with NSAIDs and ACE inhibitors.

## **Instructions for Use**

There is a specific protocol (see [dosing](#) section) that must be followed for proper use of this drug. If reductions in diet are not maintained and diet is not restricted, animals will regain weight following cessation of treatment. To avoid this rebound weight gain, it is important to continue the feeding for maintenance regimen after the end of treatment with the product. Treatment should be given with food. The appetite suppression is less in dogs that are fed a low-fat diet compared to a diet higher in fat content.

## **Patient Monitoring and Laboratory Tests**

Monitor patient's weight. Monitor blood chemistry profile for increases in liver enzymes and reduced albumin and electrolytes.

## **Formulations**

- Mitratapide is available in 5-mg/mL oral solution.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Once opened, it has a shelf life of 3 months. Do not refrigerate.

## **Small Animal Dosage**

### **Dogs**

- 0.63 mg/kg once daily (1 mL of the product per 8 kg). This dose is administered for two periods of 21 days with a break of 14 days without treatment between each period. Weighing the animal during treatment is important. Weigh the dog on day 1 and on day 35 (i.e., at the start of each treatment period). During the first 21 days of treatment, the quantity of food should not be changed. Thereafter, adjust the amount of food according to energy requirements for maintenance with a regular pet food or with a low-calorie (diet) pet food. The lower amount can be continued after treatment is discontinued.

### **Cats**

- Do not use.

## **Large Animal Dosage**

- No large animal doses have been reported.

## **Regulatory Information**

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food.

## Morphine Sulfate

mor'feen sul'fate

**Trade and other names:** Generic brands, MS Contin extended-release tablets, Oramorph SR extended-release tablets, and generic brand extended-release tablets

**Functional classification:** Analgesic, opioid

### Pharmacology and Mechanism of Action

Opioid agonist, analgesic. Prototype for other opioid agonists. Action of morphine is to bind to mu-opiate and kappa-opiate receptors on nerves and inhibit release of neurotransmitters involved with transmission of pain stimuli (such as substance P). Morphine also may inhibit release of some inflammatory mediators. The CNS effects and euphoric properties are related to mu-receptor effects in brain. Other opiates and opioids used in animals include hydromorphone, codeine, oxymorphone, meperidine, and fentanyl. Pharmacokinetics have been studied in most species. In horses, it has a short half-life (1.5-3 hours) and high clearance (30-35 mL/kg/min). In cats, it has a half-life of 76 minutes (IV) and 93 minutes (IM). Clearance in cats is 24 mL/kg/min. In dogs, the half-life is also short (1.2 hours) with high clearance (60 mL/kg/min). Oral morphine formulations are poorly bioavailable in dogs and may not be effective.

### Indications and Clinical Uses

Morphine is indicated for short-term analgesia, for sedation, and as an adjunct to anesthesia. It is compatible with most anesthetics and can be used as part of a multimodal approach to analgesia/anesthesia. Administration of morphine may lower dose requirements for other anesthetics and analgesics used. Morphine has been used in animals for treatment of pulmonary edema. Presumably, this effect is attributed to vasodilation and reduction of preload in animals. Although oral morphine (regular and sustained release) has been used in dogs, its absorption is poor and inconsistent. The oral dose formulations should not be relied on for treating severe pain in dogs. Morphine oral administration has not been investigated in cats. Injectable forms can be used in cats, but doses are generally lower than in dogs to prevent excitement. In horses, it is rarely used alone or without other sedatives because undesirable behavior and cardiovascular effects may occur at doses that are needed for analgesia. At a dose of 0.3-0.6 mg/kg to horses, it significantly increases locomotor activity, produces excitement, and decreases gastrointestinal motility. It produces colic at 1.0 mg/kg, and severe ataxia and collapse at 2.4 mg/kg. At lower doses of 0.1-0.2 mg/kg, it did not produce colic or excitement or adverse gastrointestinal effects, but these low doses were not adequate to produce analgesia.

### Precautionary Information

#### Adverse Reactions and Side Effects

Like all opiates, side effects from morphine are predictable and unavoidable. Side effects from morphine administration include sedation, vomiting, constipation, urinary retention, and bradycardia. Panting may occur in dogs as a result of changes in thermoregulation. Histamine release occurs from administration of morphine, but it may be less likely with other opioids. Excitement can occur in some animals, but it is more common in cats and horses. Respiratory depression occurs with high doses. As with other opiates, a slight decrease in heart rate is expected. In most

cases, this decrease does not have to be treated with anticholinergic drugs (e.g., atropine), but it should be monitored. Tolerance and dependence occur with chronic administration. In horses, there was ileus, constipation, and CNS stimulation (pawing and pacing) following 0.5 mg/kg. In horses, undesirable and even dangerous behavior actions can follow rapid IV opioid administration. Muscle twitching, fasciculations, and sweating also occur in horses. If used in horses, they should receive a preanesthetic of acepromazine or an  $\alpha_2$ -agonist.

### **Contraindications and Precautions**

Morphine is a Schedule II controlled substance. Cats and horses are more sensitive to excitement than other species.

### **Drug Interactions**

Like other opiates, it will potentiate other drugs that cause CNS depression.

### **Instructions for Use**

Effects from morphine administration are dose dependent. Low doses (0.1-0.25 mg/kg) produce mild analgesia. Higher doses (up to 1 mg/kg) produce greater analgesic effects and sedation. Usually morphine is administered IM, IV, or SQ. Constant-rate infusions also have been used, and doses cited below have been shown to produce morphine concentrations in a therapeutic range. Oral morphine is available in sustained-release forms, but oral dosing can be highly variable and inconsistent. Epidural administration has been used for surgical procedures. Combination protocols include MMK, which is morphine (0.2 mg/kg) + medetomidine 60 mcg/kg (or dexmedetomidine) + ketamine (5 mg/kg), all mixed in one syringe and administered intramuscularly to produce short-term analgesia and anesthesia for approximately 120 minutes. Another mixture is MLK, which is morphine (or fentanyl), lidocaine, and ketamine (see [dosing](#) section for formula).

### **Patient Monitoring and Laboratory Tests**

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, if necessary, atropine can be administered. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

### **Formulations**

- Morphine is available in 1-, 2-, 4-, 5-, 8-, 10-, 15-, 25-, and 50-mg/mL injection (most common is 15 mg/mL); 15- and 30-mg tablets; and extended-release tablets in 15, 30, 60, 100, and 200 mg (MS Contin, Oramorph SR, or generic brands). Morphine pentahydrate (Avinza) is available in 60-mg capsules.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Morphine sulfate is slightly water soluble and soluble in ethanol. It is more stable at pH <4. If mixed with high-pH vehicles, oxidation occurs, which may darken the formulation (brownish yellow). Solutions may be repackaged in plastic syringes and kept stable for 70 days. If mixed with sodium chloride (0.9%) for epidural injection, it is stable for 14 weeks. Protect from freezing.

### **Small Animal Dosage**

#### **Dogs**

- Analgesia: 0.5 mg/kg q2h IV or IM. However, a dose range of 0.1-1 mg/kg IV, IM, or SQ q4h has also been used (dose is escalated as needed).
- CRI: Loading dose of 0.2 mg/kg IV, followed by 0.1 mg/kg/hr. This may be increased to a loading dose of 0.3 mg/kg, followed by 0.17 mg/kg/hr for more severe

pain. Doses as high as a loading dose of 0.6 mg/kg, followed by 0.34 mg/kg IV have been used in experimental dogs.

- Oral dosing: Regular tablets should not be used. Sustained-release tablets have been used at a dose of 15 or 30 mg per dog q8-12h PO, but studies have shown these tablets to be inconsistently and poorly absorbed in dogs.
- Epidural: 0.1 mg/kg.
- Combination of MLK: mixed as 100 mg/mL ketamine (1.6 mL per 500 mL fluids) + 20 mg/mL lidocaine (30 mL per 500 mL fluids), and 15 mg/mL morphine (1.6 mL per 500 mL fluids) and infused at a rate of morphine: 0.24 mg/kg/hr; lidocaine: 3 mg/kg/hr; and ketamine: 0.6 mg/kg/hr, administered as CRI for perioperative analgesia.

### Cats

- Analgesia: 0.1-0.2 mg/kg IM, IV, or SQ q3-6h (or as needed).
- CRI: loading dose of 0.2 mg/kg IV, followed by 0.05-0.1 mg/kg/hour IV.
- Epidural 0.1 mg/kg diluted in saline to 0.3 mL/kg.

## Large Animal Dosage

### Horses

- For light chemical restraint, use 0.3-0.5 mg/kg IV. For more severe pain, administer 0.5-1 mg/kg IV or IM. Give IV doses slowly. Morphine may cause excitement in horses, and it is advised to first sedate with an  $\alpha_2$ -agonist or another sedative.
- Intraarticular (use preservative-free solutions): 0.05 mg/kg; start with initial concentration of 20 mg/mL solution and dilute in saline to 5 mg/mL and administered at a rate of 1 mL per joint per 100 kg of body weight.

### Ruminants

- The benefits of using morphine in ruminants are controversial. However, 0.05-0.1 mg/kg IV and up to 0.4 mg/kg IV have been used to treat pain and in perioperative situations.

## Regulatory Information

Morphine is a Schedule II controlled drug.

Avoid use in animals intended for food.

RCI Classification: 1

## Moxidectin

moks-ih-dek'tin

**Trade and other names:** ProHeart (canine), Coraxis, Quest (equine), and Cydectin (bovine and ovine)

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Antiparasitic drug in the milbemycin class. Avermectins (ivermectin-like drugs) and milbemycins (milbemycin and moxidectin) are macrocyclic lactones and share similarities, including mechanism of action. Compared to ivermectin, moxidectin is 100 times more lipophilic. These drugs are neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Paralysis and death of the parasite are caused by increased permeability to chloride ions and hyperpolarization of nerve cells. These drugs also potentiate other chloride channels, including ones gated by GABA, but GABA-mediated mechanism may not be important for parasites. Mammals ordinarily are not

affected because they lack glutamate-gated chloride channels, and there is a lower affinity for other mammalian chloride channels. Because these drugs ordinarily do not penetrate the blood–brain barrier, GABA-gated channels in the CNS of mammals are not affected. Moxidectin is active against intestinal parasites, mites, bots, heartworm microfilaria, and developing larvae. Moxidectin has no effect on trematode or cestode parasites. One of the equine formulations also contains praziquantel to control additional parasites.

## Indications and Clinical Uses

Moxidectin is used in dogs to prevent infection of heartworm (*Dirofilaria immitis*). In dogs it can also be used and for the treatment and control of *Ancylostoma caninum*, *Uncinaria stenocephala*, *Toxocara canis*, *Toxascaris leonina*, and *Trichuris vulpis*. Moxidectin also has been used to treat *Demodex* infections in dogs. In cats it is used for the prevention of heartworm disease caused by *Dirofilaria immitis*; for the treatment and control of intestinal roundworms (*Toxocara cati*), and hookworms (*Ancylostoma tubaeforme*). In horses, it is used for treatment of a variety of parasites, including large strongyles (*Strongylus vulgaris* [adults and L4/L5 arterial stages], *S. edentatus* [adult and tissue stages], *Triodontophorus brevicauda* [adults], and *T. serratus* [adults]); small strongyles ([adults] *Cyathostomum* spp., *Cylicocyclus* spp., *Cylicocostephanus* spp., *Coronocyclus* spp., and *Gyallocephalus capitatus*). It is also used to treat small strongyles, including larvae. It is used to treat ascarids, including *Parascaris equorum* (adults and L4 larval stages), pinworms (*Oxyuris equi* [adults and L4 larval stages]), hairworms (*Trichostrongylus axei* [adults]), large-mouth stomach worms (*Habronema muscae* [adults]), and horse stomach bots (*Gasterophilus intestinalis* [second and third instars] and *G. nasalis* [third instars]). One dose also suppresses strongyle egg production for 84 days. Some formulations for horses also contain praziquantel. This increases the spectrum to include other intestinal parasites such as tapeworms.

In cattle, moxidectin injectable is used to treat intestinal roundworms (*Ostertagia ostertagi* [adults and inhibited fourth-stage larvae], *Haemonchus placei* [adults], *Trichostrongylus axei* [adults], *T. colubriformis* [fourth-stage larvae], *Cooperia oncophora* [adults], *C. punctata* [adults and fourth-stage larvae], *C. surnabada* [adults and fourth-stage larvae], *Oesophagostomum radiatum* [adults and fourth-stage larvae], *Trichuris* spp. [adults]), lungworms (*Dictyocaulus viviparus* [adults and fourth-stage larvae]), grubs (*Hypoderma bovis* and *H. lineatum*), mites (*Psoroptes ovis* [*P. communis* var. *bovis*]), and lice (*Linognathus vituli* and *Solenopotes capillatus*). One injection will protect cattle from reinfection with *D. viviparus* and *O. radiatum* for 42 days, *H. placei* for 35 days, and *O. ostertagi* and *T. axei* for 14 days after treatment. In sheep, the oral drench is used for the treatment and control of the adult and L4 larval stages of *Haemonchus contortus*, *Teladorsagia circumcincta*, *T. trifurcata*, *Trichostrongylus axei*, *T. colubriformis*, *T. vitrinus*, *Cooperia curticei*, *C. oncophora*, *Oesophagostomum columbianum*, *O. venulosum*, *Nematodirus battus*, *N. filicollis*, and *N. spathiger*.

## Precautionary Information

### Adverse Reactions and Side Effects

Toxicity is the result of potentiation of glutamate-gated chloride channels and GABA channels resulting in hyperpolarization of membranes. Toxicity may occur at high doses and in breeds in which moxidectin crosses the blood–brain barrier. Sensitive breeds may include collies, Australian shepherds, Old English sheepdogs, longhaired whippets, and Shetland sheepdogs. Toxicity is neurotoxic, and signs include depression, ataxia, difficulty with vision, coma, and death. Sensitivity to moxidectin occurs in certain breeds because of a mutation in the ABCB1 gene that codes for the membrane pump P-glycoprotein. This mutation affects the efflux

pump in the blood–brain barrier. Adverse effects may occur when high doses of moxidectin are used to treat dogs for demodicosis. These effects include lethargy, depressed appetite, vomiting, and lesions at the site of an SQ injection. Toxicity is more likely at high doses in dogs. At five times the label dose rate (15 mcg/kg) once every month, moxidectin was administered safely to collies that were ivermectin sensitive. However, at a single dose of 90 mcg/kg (30 times the label dose) administered to sensitive collies, ataxia, lethargy, and salivation occurred in one sixth of dogs. At 30, 60, and 90 mcg/kg to ivermectin-sensitive collies (10 times, 20 times, and 30 times the label dose), no adverse effects were observed. Nevertheless, caution is advised when administering moxidectin to sensitive breeds listed previously. Because of concern about adverse reactions and deaths in dogs from the 6-month injectable formulation (ProHeart 6), this product was temporarily discontinued. The safety concerns have been addressed by reformulating the product, which is now available. In horses, moxidectin has been safe at three times the label dose. However, adverse effects (ataxia, depression, and lethargy) have been reported in young horses (younger than 6 months) or debilitated animals after treatment. Other adverse effects reported in horses include sedation, weakness, bradycardia, dyspnea, coma, and seizures.

Neurological toxicity in animals producing seizures can be treated with diazepam, barbiturates, or propofol.

### Contraindications and Precautions

Do not use in dogs younger than 2 months of age. The canine long-acting formulation ProHeart 6 was temporarily discontinued but reintroduced after reformulation. Despite the safety margin listed in the “Adverse Reactions and Side Effects” section, caution is advised when administering moxidectin at high doses to ivermectin-sensitive breeds. Affected breeds may include collies, Australian shepherds, Old English sheepdogs, longhaired whippets, and Shetland sheepdogs. Administration to foals younger than 6 months of age is not recommended. Do not apply the pour-on formulation to small animals. It has been used safely in queens and kittens during pregnancy and lactation.

### Drug Interactions

Do not administer with drugs that could potentially increase the penetration of ivermectin across the blood–brain barrier. Such drugs include ketoconazole, itraconazole, cyclosporine, and calcium-channel blockers (See Appendix J).

## Instructions for Use

Caution is recommended if bovine or equine formulation is considered for use in small animals. Toxic overdoses are likely because these formulations are highly concentrated.

## Patient Monitoring and Laboratory Tests

Animals should be checked for heartworm status prior to initiating treatment.

## Formulations

- Moxidectin is available in 30-, 68-, and 136-mcg tablets for dogs; 20-mg/mL equine oral gel; 5-mg/mL cattle pour-on; 1-mg/mL oral drench for sheep; 10-mg/mL injectable solution for cattle; and Quest 2% gel for horses (20 mg/mL). Quest Plus gel for horses contains 20 mg/mL (2%) plus 125 mg praziquantel (12.5%). The 6-month injectable (ProHeart 6) formulation consists of two separate vials: one contains 10% moxidectin microspheres, and the other contains a vehicle for constitution of the moxidectin microspheres. Each milliliter of constituted, sustained-release suspension contains 3.4 mg of moxidectin. The formulation Advantage Multi for dogs 2.5% (25mg/mL) includes 25% Imidacloprid. Advantage Multi for cats 1% (10mg/mL) includes 10% Imidacloprid.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs**

- Heartworm prevention: 3 mcg/kg every 30 days PO. Topical heartworm prevention (Advantage Multi) 2.5mg/kg monthly.
- Heartworm prevention (long-acting injectable): 0.17 mg/kg (170 mcg/kg) SQ as a single dose.
- Endoparasite control: 25-300 mcg/kg.
- Sarcoptic mange: 200-250 mcg/kg (0.2-0.25 mg/kg) PO or SQ once per week for 3-6 weeks.
- Demodicosis: 200 mcg/kg SQ weekly or every other week for 1-4 doses; alternatively, higher doses of 400 mcg/kg/day PO. Higher doses are used for refractory *Demodex* cases, with doses of 500 mcg/kg (0.5 mg/kg)/day PO for 21-23 weeks or 0.5-1.0 mg/kg SQ q72h for 21-22 weeks. Duration of treatment for demodicosis is variable. Treat until two negative *Demodex* skin scrapings are achieved.

**Cats**

- Topical heartworm prevention with Advantage Multi is 1 mg/kg of moxidectin topically every 30 days

**Large Animal Dosage****Horses**

- Gastrointestinal parasites: 0.4 mg/kg PO. Avoid use in young horses, small ponies, or debilitated animals.

**Cattle**

- 0.2 mg/kg SQ once.
- Intestinal parasites, lungworms, mites, grubs, and lice: Topical treatment (pour-on): 0.5 mg/kg (0.23 mg/lb or 45 mL per 1000 lbs). Apply topically along the midline from the withers to the tail head. Avoid exposure to human skin and to other animals.

**Sheep**

- 1 mL per 5 kg (1 mL per 11 pounds, or 0.2 mg/kg) by mouth of the 1-mg/mL oral solution.

**Regulatory Information**

Do not use in horses intended for food.

Cattle withdrawal time (meat): 21 days.

Sheep withdrawal time (meat): 7 days.

Goat withdrawal time (meat): 14 days.

No milk withholding time has been established. Do not use in female dairy cattle of breeding age. Do not use in female sheep providing milk for human consumption.

Do not use in veal calves.

**Moxifloxacin**

moks-ih-floks'ah-sin

**Trade and other names:** Avelox

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Fluoroquinolone antibacterial. Moxifloxacin, like other quinolones, inhibits DNA gyrase and prevents bacterial cell DNA and RNA synthesis. Moxifloxacin is bactericidal with broad antimicrobial activity. It has a chemical structure slightly different from older veterinary fluoroquinolones (8 methoxy substitution). As a result of this modification, this newer generation of drugs, such as moxifloxacin, has greater activity against gram-positive bacteria and anaerobes than the veterinary fluoroquinolones (enrofloxacin, orbifloxacin, and marbofloxacin). An approved veterinary drug with a similar spectrum is pradofloxacin. Pradofloxacin may be used in animals instead of moxifloxacin for some indications.

## Indications and Clinical Uses

Moxifloxacin, although a human drug, has been used in small animals for treatment of infections refractory to other drugs, including skin infections, pneumonia, and soft tissue infections. The spectrum of activity includes gram-positive cocci and anaerobic bacteria that may be resistant to other quinolones. Because other veterinary fluoroquinolones are preferred for initial use (enrofloxacin, orbifloxacin, and marbofloxacin), moxifloxacin use is not common. Data for use in small animals are sparse, and regimens are primarily extrapolated from the human label. In horses, it has been administered at 5.8 mg/kg/day for 3 days. Although pharmacokinetics were favorable in horses, it caused diarrhea that may present a risk.

## Precautionary Information

### Adverse Reactions and Side Effects

High concentrations may cause CNS toxicity, especially in animals with kidney disease. Moxifloxacin causes occasional vomiting. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4 to 28 weeks of age. Large, rapidly growing dogs are the most susceptible. In horses, moxifloxacin at high doses caused diarrhea and is not recommended for routine use. Moxifloxacin at high doses has caused a dose-related prolongation of the Q-T interval. The clinical consequences of this observation for animals are not known.

### Contraindications and Precautions

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures. Avoid use in horses, rodents, and rabbits because of risk of diarrhea.

### Drug Interactions

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

## Instructions for Use

Doses are based on plasma concentrations needed to achieve sufficient plasma concentration above the MIC value. Efficacy studies have not been performed in dogs or cats.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for sensitive organisms are  $\leq 1.0$  mcg/mL. Most sensitive gram-negative bacteria of the *Enterobacteriaceae* have MIC values  $\leq 0.1$  mcg/mL.

## Formulations

- Moxifloxacin is available in 400-mg tablets.



**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Do not mix with products that contain ions (iron, aluminum, magnesium, and calcium).

**Small Animal Dosage****Dogs and Cats**

- 10 mg/kg q24h PO.

**Large Animal Dosage****Horses**

- 5.8 mg/kg q24h for 3 days, but it caused diarrhea. Therefore there may be risks with long-term use.

**Regulatory Information**

There are no withdrawal times established because this drug should not be administered to animals that produce food.

**Mycophenolate Mofetil**

mye-koe-fen'oh-late

**Trade and other names:** CellCept

**Functional classification:** Immunosuppressant

**Pharmacology and Mechanism of Action**

Mycophenolate is an ester prodrug metabolized to mycophenolic acid (MPA). It is used to suppress immunity for transplantation and for treatment of immune-mediated diseases. Mycophenolate, when metabolized to MPA, inhibits inosine monophosphate dehydrogenase (IMPDH), which is an important enzyme for the de novo synthesis of purines in immune cells, especially stimulated lymphocytes. T- and B-lymphocytes are critically dependent on de novo synthesis of purine nucleotides. Therefore it effectively suppresses T- and B-cell lymphocyte proliferation and decreases antibody synthesis by B-cells. In people, it is used as a replacement for azathioprine and has been primarily used for immune suppression in patients undergoing liver or kidney transplants, but other uses are being explored. It is usually used in combination with glucocorticoids and/or cyclosporine. The half-life in dogs is only 45 minutes, but it is longer for the metabolite, with a half-life of 2.2-4.6 hours and as long as 8 hours for the metabolite in some dogs.

**Indications and Clinical Uses**

Mycophenolate is used to treat immune-mediated diseases in animals. It is usually used in veterinary medicine (primarily dogs and cats) when other agents such as azathioprine, chlorambucil, or glucocorticosteroids alone fail to achieve remission of an immune-mediated disease. In dogs, mycophenolate has been used on a limited basis to treat some immune-mediated diseases such as aplastic anemia, immune-mediated hemolytic anemia, and autoimmune skin disease. The response in these diseases is based on anecdotal accounts and has been variable. In dogs the active metabolite (MPA) is produced in highly variable concentrations, which may explain the variable results observed in dogs. It has been used by neurologists for treatment of myasthenia gravis, but one clinical report indicated that it was not effective. According to pharmacokinetic studies with mycophenolate in dogs, the elimination rate was rapid (half-life less than 1 hour), which may require frequent dosing in dogs for successful therapy. For treatment of pemphigus

foliaceous, it was given at a dose of 22-39 mg/kg/day divided into three treatments. It was well tolerated, but only three out of eight dogs completed the study and were improved. Azathioprine is more commonly used as an immunosuppressive agent. In cats, the use is limited and only based on small case studies or anecdotal reports. It has been used for some immune-mediated diseases in cats, with uncertain efficacy.

## Precautionary Information

### Adverse Reactions and Side Effects

In dogs, gastrointestinal problems (diarrhea, weight loss, anorexia, and vomiting) have been the most common effects reported, which may be caused by a direct effect on intestinal mucosa. At the low dose of 10 mg/kg, it may not be effective, but as dose is increased to 30 mg/kg, adverse gastrointestinal effects are more common (nausea, diarrhea, weight loss). In cats at 10 mg/kg PO q12h, it was well tolerated.

### Contraindications and Precautions

Mycophenolate is an immunosuppressive drug. Patients will be more prone to infection when receiving mycophenolate.

### Drug Interactions

Some drug interactions that affect oral bioavailability in humans have been reported (e.g., antibiotics, cyclosporine, antacid drugs), but these drug interactions have not been recognized in animals. It is frequently administered with corticosteroids.

## Instructions for Use

Mycophenolate is used in some patients that cannot tolerate other immunosuppressive drugs, such as azathioprine or cyclophosphamide. It has been used in combination with corticosteroids and cyclosporine.

## Patient Monitoring and Laboratory Tests

Monitor for signs of infection in patients. Monitor CBC periodically when administering immunosuppressive agents.

## Formulations

- Mycophenolate is available in 250- and 500-mg capsules.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is slightly soluble in water. It is more stable at low pH values (<4). It may be prepared in a syrup suspension for flavoring and remains stable for 121 days.

## Small Animal Dosage

### Dogs

- 10 mg/kg q8h PO, or 20 mg/kg q 8-12h PO. (As dose is increased, adverse effects are more common.)

### Cats

- 10 mg/kg q12h PO.

## Large Animal Dosage

- No large animal dose has been reported.

## Regulatory Information

There are no withdrawal times established because this drug should not be administered to animals that produce food.

## Naloxone Hydrochloride

nal-oks'one hye-droe-klor'ide

**Trade and other names:** Narcan and Trexonil

**Functional classification:** Opioid antagonist

### Pharmacology and Mechanism of Action

Opiate antagonist. Naloxone competes for opiate receptors and displaces opioid drugs from these receptors, thus reversing their effects. Naloxone is capable of antagonizing all opiate receptors.

### Indications and Clinical Uses

Naloxone is used to reverse the effects of opiate agonists on receptors. Naloxone is used to reverse overdoses or toxicity. It will reverse effects of morphine, oxymorphone, buprenorphine, hydromorphone, and other opioids. It is less effective for reversing buprenorphine because buprenorphine is a partial agonist. When administering naloxone to reverse opiates, it may be titrated in gradually to achieve the optimum amount of reversal.

The dose for full reversal is typically 0.04 mg/kg (40 mcg/kg), but doses this high may not be needed, and smaller doses—producing partial reversal—are often recommended. At very low doses (one fifth of the dose needed to fully reverse opiates), it has been used to treat opioid-induced side effects such as vomiting, nausea, and dysphoria. (This use has been referred to as microdosing.) A formulation for wildlife use (Trexonil) is more concentrated and used to reverse tranquilization in wild animals. Naloxone may have some temporary benefit for behavior modification (e.g., to suppress compulsive disorders), but the effects are short lived. For example, in horses, it will temporarily decrease crib biting, but the duration of action is short.

### Precautionary Information

#### Adverse Reactions and Side Effects

Tachycardia and hypertension have been reported in people. In animals, reversal of opioid may precipitate a severe reaction that includes high blood pressure, excitement, pain, tachycardia, and cardiac arrhythmias. Because of these reactions, less than a full reversal often is recommended, unless the reversal is needed for a life-threatening problem.

#### Contraindications and Precautions

Administration to an animal that is experiencing pain will precipitate extreme reactions because of blockade of endogenous opioids.

#### Drug Interactions

Naloxone will reverse the action of other opioid drugs.

### Instructions for Use

Administration may have to be individualized based on response in each patient. Naloxone's duration of action is short in animals (60 minutes), and it may have to be readministered. Start at the low end of the dosage rate and increase the dose to effect. Higher doses may be needed to reverse drugs that are mixed agonists/antagonists such as butorphanol or buprenorphine, compared to reversing drugs that are pure agonists. Low doses may be used to reduce opioid-induced dysphoria in animals. For this use, start with 0.04 mg/mL solution and administer increments of

1 mL every 30 seconds until vocalization or signs of dysphoria stop. A dose of 0.01 mg/kg IV has been given for this purpose without losing analgesic effects.

A dose of 1 mL (0.4 mg) will reverse 1.5 mg oxymorphone, 15 mg morphine, 100 mg meperidine, and 0.4 mg fentanyl.

### Patient Monitoring and Laboratory Tests

Naloxone is used to reverse opioid analgesic drugs. When opioids are reversed in some animals, serious reactions may occur. In some patients, changes in blood pressure, tachycardia, and discomfort may result.

### Formulations Available

- Naloxone is available in injectable vials with preservatives in 0.4 or 1 mg/mL; without preservatives in 0.02 mg (20 mcg), 0.4 mg, or 1 mg per mL; and as Trexonil in 50 mg/mL.

### Stability and Storage

When used intravenously, it may be diluted in other fluids. For IV infusion, it may be added to 0.9% sodium chloride solution or 5% dextrose solution. An amount of 2 mg of naloxone may be mixed with 500 mL of fluids to produce 4 mcg/mL. After dilution it should be used within 24 hours. Do not mix with other drugs or solutions that are alkaline. Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 0.01-0.04 mg/kg IV, IM, or SQ as needed to reverse opiate.
- Low dose to partially reverse dysphoric reaction: Administer 1 mL every 30 seconds (0.04 mg/mL solution) as needed.

### Large Animal Dosage

#### Horses

- 0.02-0.04 mg/kg IV (duration of effect is only 20 minutes).

### Regulatory Information

No withdrawal times are established. It is anticipated that naloxone is cleared rapidly after administration. Because of low risk of residues, short (24-48 hour) withdrawal times are suggested.

Racing Commissioners International (RCI) Classification: 3

## Naltrexone

nal-treks'one

**Trade and other names:** Trexan, Vivitrol

**Functional classification:** Opioid antagonist

### Pharmacology and Mechanism of Action

Opiate antagonist. Naltrexone competes for opiate receptors and displaces opioid drugs from these receptors, thus reversing their effects. It is capable of antagonizing all opiate receptors. Its action is similar to naloxone except that it is longer acting and administered orally. A related drug that does not have central-acting effects is methylnaltrexone (used to treat intestinal ileus). For humans, there is a long-acting

injection formulated in microspheres that persists for 1 month after a single injection. The long-acting form has not been used in animals.

### **Indications and Clinical Uses**

Naltrexone is used in people for treatment of opiate dependence and alcoholism. In animals, some obsessive-compulsive disorders are believed to be mediated by endogenous opioids. It has been used successfully for treatment of some obsessive-compulsive behavioral disorders, such as tail chasing in dogs, acral lick granuloma in dogs, and crib biting in horses. The effect for each of these disorders is short lived.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects have not been reported in animals. In people, it can precipitate opioid withdrawal signs.

#### **Contraindications and Precautions**

Do not administer to animals in pain, or it may elicit a severe reaction.

#### **Drug Interactions**

Naltrexone will reverse the action of other opioid drugs.

### **Instructions for Use**

For acute treatment of opiate toxicity, use naloxone instead because it can be injected with a more rapid onset of effects. Treatment for obsessive-compulsive disorders (canine compulsive disorder) in animals has been reported with naltrexone. Relapse rates may be high.

### **Patient Monitoring and Laboratory Tests**

Monitor heart rate in treated animals.

### **Formulations**

- Naltrexone is available in 50-mg tablets. Vivitrol for humans is an encapsulated microsphere that can be injected to produce a long-lasting effect (one injection per month) to treat substance dependence. One vial contains 380 mg in microspheres in a 4-mL injection for IM use.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Naltrexone is soluble in water. It has been mixed with juices and syrups to mask the bitter taste and was stable for 60-90 days.

### **Small Animal Dosage**

#### **Dogs**

- For behavior problems: 2.2 mg/kg q12h PO.

### **Large Animal Dosage**

#### **Horses**

- Crib biting: 0.04 mg/kg IV or SQ. (Because injectable formulations are not available, it must be compounded for this indication.) Duration of effect is 1-7 hours.
- For reversal of opiates: 100 mg/animal IV or SQ. (Because injectable formulations are not available, it must be compounded for this indication.)

### **Regulatory Information**

Withdrawal times are not established for animals that produce food. In wild animals that are captured with opiates and administered naltrexone for reversal, a 45-day withdrawal

time is suggested. For additional extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).  
RCI Classification: 3

## Nandrolone Decanoate

nan'droe-lone dek-ah-noe'ate

**Trade and other names:** Deca-Durabolin

**Functional classification:** Hormone, anabolic agent

### Pharmacology and Mechanism of Action

Anabolic steroid. Nandrolone is a derivative of testosterone used as an anabolic agent. Anabolic agents are designed to maximize anabolic effects while minimizing androgenic action.

### Indications and Clinical Uses

Anabolic agents have been used for reversing catabolic conditions, promoting weight gain, increasing muscling in animals, and stimulating erythropoiesis. There are no differences in efficacy among the anabolic steroids reported in animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects from anabolic steroids can be attributed to the pharmacologic action of these steroids. Increased masculine effects are common. There has been an increased incidence of some tumors in people. Some of the oral anabolic steroids that are 17 alpha-methylated (oxymetholone, stanozolol, and oxandrolone) are associated with hepatic toxicity.

#### Contraindications and Precautions

Use cautiously in patients with hepatic disease. Do not use in pregnant animals.

#### Drug Interactions

No drug interactions have been reported.

### Instructions for Use

Results of clinical studies in animals have not been reported. Nandrolone use in animals (and doses) is based on experience in people or anecdotal experience in animals.

### Patient Monitoring and Laboratory Tests

Monitor liver enzymes in treated patients.

### Formulations

- Nandrolone decanoate is available in 50-, 100-, and 200-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 1-1.5 mg/kg/wk IM.

#### Cats

- 1 mg/kg/wk IM.

## Large Animal Dosage

### Horses

- 1 mg/kg q4wk IM.

## Regulatory Information

Nandrolone is a Schedule III controlled drug.

Do not administer to animals intended for food.

RCI Classification: 4

## Naproxen

nah-proks'en

**Trade and other names:** Naprosyn, Naxen, and Aleve (naproxen sodium)

**Functional classification:** Nonsteroidal anti-inflammatory drug (NSAID)

## Pharmacology and Mechanism of Action

Naproxen and other NSAIDs have produced analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclooxygenase (COX) enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy GI tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, there are overlapping functions of the mediators derived from these isoforms. Naproxen is a nonselective inhibitor of COX-1 and COX-2. The pharmacokinetics of naproxen in dogs and horses differ substantially from people. Whereas in people the half-life is approximately 12-15 hours, the half-life in dogs is 35-74 hours and in horses is only 4-8 hours, which can lead to toxicity in dogs and brief duration of effects in horses.

## Indications and Clinical Uses

Naproxen is approved for use in people and is popular for treating osteoarthritis. It has been used for treatment of musculoskeletal problems, such as myositis and osteoarthritis in dogs and horses. There are no veterinary formulations marketed. Its use has diminished because there are FDA-approved drugs for these indications for horses and dogs.

## Precautionary Information

### Adverse Reactions and Side Effects

Naproxen is a potent NSAID. Adverse effects attributed to GI toxicity are common to all NSAIDs. Naproxen has produced serious ulceration in dogs because elimination in dogs is many times slower than in people or horses. Kidney injury caused by renal ischemia also is possible with repeated doses.

### Contraindications and Precautions

Caution is advised when using the over-the-counter (OTC) formulation designed for people because the tablet size is much larger than the safe dose for dogs. Therefore warn pet owners about administration to dogs without consulting a veterinarian first. Dosing rates for people are not appropriate for dogs. Do not administer to animals prone to gastrointestinal (GI) ulcers. Do not administer with other ulcerogenic drugs, such as corticosteroids.

### Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and angiotensin-converting enzyme (ACE) inhibitors.

### Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on pharmacokinetic studies in experimental animals.

### Patient Monitoring and Laboratory Tests

Monitor for signs of GI ulceration.

### Formulations

- Naproxen is available in 220-mg tablets (OTC). (A 220-mg dose of naproxen sodium is equivalent to 200 mg naproxen.) It is also available in 25-mg/mL oral suspension and 250-, 375-, and 500-mg tablets (prescription).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Naproxen is practically insoluble in water at low pH, but it increases at high pH. It is soluble in ethanol.

### Small Animal Dosage

#### Dogs

- 5 mg/kg initially, then 2 mg/kg q48h PO.

### Large Animal Dosage

#### Horses

- 10 mg/kg q12h PO.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 4

## N-Butylscopolammonium Bromide (Butylscopolamine Bromide)

en-byoo-til-skoe-pahl'ah-moe-nee-um broe'mide

**Trade and other names:** Buscopan

**Functional classification:** Antispasmodic

### Pharmacology and Mechanism of Action

Antispasmodic, antimuscarinic, anticholinergic drug. This is a quaternary ammonium compound derived from belladonna alkaloid. Butylscopolamine, like other antimuscarinic drugs, blocks cholinergic receptors and produces a parasympatholytic effect. It affects receptors throughout the body, but it is used more commonly for its gastrointestinal (GI) effects. It effectively inhibits secretions and motility of the GI tract by blocking parasympathetic receptors. It has a short half-life (15-25 minutes) and short duration of action.



## Indications and Clinical Uses

Butylscopolamine bromide is indicated for treating pain associated with spasmodic colic, flatulent colic, and intestinal impactions in horses. It is also used to relax the rectum and reduce intestinal strain to facilitate diagnostic rectal palpation. Because of effects to relax smooth muscle via anticholinergic mechanisms, it is effective for short-term treatment (usually one injection) to horses with recurrent airway obstruction (also known as “heaves”).

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse reactions from anticholinergic drugs are related to their blocking of acetylcholine receptors and producing a systemic parasympatholytic response. As expected with this class of drugs, animals will have increased heart rate, decreased secretions, dry mucous membranes, decreased GI tract motility, and dilated pupils. In target animal safety studies in which doses of 1, 3, and 5 times the approved dose and up to 10 times the dose were administered to horses, the clinical signs described previously were observed. However, at high doses there were no complete blood count (CBC) or biochemical abnormalities or lesions identified at necropsy.

### Contraindications and Precautions

N-butylscopolammonium bromide will decrease intestinal motility. Use cautiously in conditions where decreased motility will be a concern.

### Drug Interactions

N-butylscopolammonium bromide is an anticholinergic drug and therefore will antagonize any other medications that are intended to produce a cholinergic response (e.g., metoclopramide).

## Instructions for Use

Experience is limited to treating spasmodic colic, flatulent colic, and intestinal impactions in horses. There is no experience in other animals.

## Patient Monitoring and Laboratory Tests

Monitor equine intestinal motility (gut sounds and fecal output) during treatment. Monitor heart rate in treated animals.

## Formulations

- N-butylscopolammonium is available in a 20-mg/mL solution.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

- No dose is reported for small animals.

## Large Animal Dosage

### Horses

- 0.3 mg/kg, slowly IV as a single dose (1.5 mL per 100 kg).

## Regulatory Information

Do not administer to animals intended for food.

## Neomycin

nee-oh-mye'sin

**Trade and other names:** Biosol

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Aminoglycoside antibiotic. The action of neomycin is to inhibit bacteria protein synthesis via binding to 30S ribosome. It is bactericidal with a broad spectrum of activity except against streptococci and anaerobic bacteria. Neomycin differs from other aminoglycosides because it is only administered topically or orally. Systemic absorption is minimal from oral absorption.

### Indications and Clinical Uses

Neomycin is only available in topical formulations. It is often combined with other antibiotics (triple antibiotics) in ointments for topical treatment of superficial infections. It is also used locally (oral local) for treatment of intestinal infections (colibacillosis). It is given orally and, because it is not absorbed systemically, produces a local effect.

### Precautionary Information

#### Adverse Reactions and Side Effects

Although oral absorption is so small that systemic adverse effects are unlikely, some oral absorption has been demonstrated in young animals (calves). Alterations in intestinal bacterial flora from therapy may cause diarrhea.

#### Contraindications and Precautions

Use cautiously in animals with kidney disease. If oral absorption occurs because of compromised mucosal integrity, absorption may occur from the intestine. Do not use longer than 14 days. Neomycin has been mixed with water and injected, but this practice is strongly discouraged.

#### Drug Interactions

Neomycin should not be mixed with other drugs before administration. Other drugs may bind and become inactivated.

### Instructions for Use

Efficacy for treatment of diarrhea, especially for nonspecific diarrhea, is questionable.

### Patient Monitoring and Laboratory Tests

Monitor for signs of diarrhea. If sufficiently absorbed systemically, it could cause kidney injury; therefore monitor blood urea nitrogen (BUN) and creatinine with chronic use.

### Formulations

- Neomycin is available in 500-mg bolus, 50-mg/mL (equivalent to 35 mg/mL of neomycin base) and 200-mg/mL oral liquid (equivalent to 140 mg/mL of neomycin base), and 325-mg soluble powder (equivalent to 20.3 g per ounce of neomycin base).

### Stability and Storage

It may be added to drinking water or milk. Do not add to other liquid supplements. Prepare a fresh solution daily. It is freely soluble in water and slightly soluble in ethanol. Aqueous solutions are stable over a wide pH range with optimum stability at pH 7. Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats**

- 10-20 mg/kg q6-12h PO.

**Large Animal Dosage****Calves, Sheep, Goats, Pigs**

- 22 mg/kg/day PO.

**Regulatory Information**

Slaughter withdrawal times: cattle, 1 day; sheep, 2 days; swine and goats, 3 days. Oral administration may cause residues in animals intended for food; therefore do not administer to veal calves.

**Neostigmine**

nee-oh-stig'meen

**Trade and other names:** Prostigmin, Stiglyn, Neostigmine bromide, and Neostigmine methylsulfate

**Functional classification:** Anticholinesterase

**Pharmacology and Mechanism of Action**

Cholinesterase inhibitor. Anticholinesterase drug and antimuscarinic drug. This drug inhibits the enzyme that metabolizes acetylcholine into inactive products. Therefore it prolongs the action of acetylcholine at the synapse. The major difference between physostigmine and neostigmine or pyridostigmine is that physostigmine crosses the blood-brain barrier and the others do not.

**Indications and Clinical Uses**

Neostigmine is used as an antidote for anticholinergic intoxication. It is also used as a treatment for myasthenia gravis, treatment (antidote) for neuromuscular blockade, and treatment for ileus. It also has been used as a treatment of urinary retention—such as the retention observed in postoperative patients—by increasing the tone of bladder smooth muscle. In ruminants, it has been used to stimulate rumen and intestinal motility. In horses, it has been used to stimulate GI motility, but results have been mixed. It may increase intestinal motility and increase fecal output, but may not increase stomach emptying.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are caused by the cholinergic action resulting from inhibition of cholinesterase. These effects can be seen in the GI tract as diarrhea and increased secretions. Other adverse effects can include miosis, bradycardia, muscle twitching or weakness, and constriction of bronchi and ureters. Adverse effects can be treated with anticholinergic drugs such as atropine. Pyridostigmine may be associated with fewer adverse effects than neostigmine.

**Contraindications and Precautions**

Do not use in urinary obstruction, intestinal obstruction, asthma or bronchoconstriction, pneumonia, and cardiac arrhythmias. The administration to horses is

discouraged because it may increase abdominal discomfort. Do not use in patients sensitive to bromide. If the patient is also receiving bromide (e.g., KBr) for treatment of seizures, this formulation may contribute to excess bromide administration.

### Drug Interactions

Do not use with other cholinergic drugs. Anticholinergic drugs (atropine and glycopyrrolate) will block the effects.

### Instructions for Use

Neostigmine is indicated primarily only for treatment of intoxication. For routine systemic use of an anticholinesterase drug, pyridostigmine may have fewer side effects. When neostigmine is used, frequency of dose may be increased based on observation of effects.

### Patient Monitoring and Laboratory Tests

Monitor GI signs, heart rate, and rhythm.

### Formulations

- Neostigmine bromide is available in 15-mg tablets, and neostigmine methylsulfate is available in 0.25-, 0.5-, and 1-mg/mL injections.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 2 mg/kg per day PO in divided doses.
- Antimyasthenic treatment: 10 mcg/kg IM or SQ as needed.
- Antidote for neuromuscular blockade: 40 mcg/kg IM or SQ.
- Diagnostic aid for myasthenia: 40 mcg/kg IM or 20 mcg/kg IV.

### Large Animal Dosage

When used as a treatment for neuromuscular blocking agents (cholinesterase inhibitor), the frequency of administration is determined by clinical response.

#### Horses

- 0.02-0.04 mg/kg (20-40 mcg/kg) IV or SQ. It may be delivered by constant-rate infusion (CRI) at a dose of 0.008 mg/kg/hour.

#### Cattle

- 22 mcg/kg (0.022 mg/kg) SQ.

#### Sheep

- 22-33 mcg/kg (0.022-0.033 mg/kg) SQ.

#### Swine

- 44-66 mcg/kg (0.044-0.066 mg/kg) IM.

#### Ruminants

- Stimulate rumen motility: 0.02 mg/kg IM or SQ.

### Regulatory Information

Withdrawal times are not established for animals that produce food. When used to stimulate rumen motility, no withdrawal time has been used. For additional extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 3

## Niacinamide

nye'ah-sin'ah-mide

**Trade and other names:** Nicotinamide and vitamin B<sub>3</sub>**Functional classification:** Anti-inflammatory

### Pharmacology and Mechanism of Action

Immunosuppressant. Use primarily to treat skin diseases, such as discoid lupus erythematosus and pemphigus erythematosus in dogs. Mechanism of action is not entirely known. Niacinamide may have some anti-inflammatory action such as suppression of inflammatory cells. Niacin and niacinamide are also used to treat vitamin B<sub>3</sub> deficiency. Do not confuse niacin with niacinamide. Niacin is converted to the active form niacinamide by intestinal bacteria.

Niacin is used in people as a lipid-regulating compound used to lower circulating blood triglycerides (TGs) and reduce low-density lipoproteins (LDL). The primary treatment in people for niacin is to treat dyslipidemias.

### Indications and Clinical Uses

Niacinamide has been used to treat immune-mediated skin disease in small animals. For skin disorders, it is usually administered with tetracycline. It also has been used to treat vitamin B<sub>3</sub> deficiency. Use in animals has been primarily derived from a few clinical reports and empirical use.

### Precautionary Information

#### Adverse Reactions and Side Effects

Side effects are not common but have included vomiting, anorexia, lethargy, and diarrhea. In people, when niacin is administered to treat dyslipidemias, side effects are common, which includes flushing of skin. The flushing effect of niacin is thought to occur through skin prostaglandin induction and activation of prostaglandin-associated receptors. When activated, the niacin receptor functions by increasing prostaglandin synthesis and activation of vasodilatory prostaglandin receptors in the skin. In people, niacin also has been associated with liver injury.

#### Contraindications and Precautions

No contraindications are reported for animals.

#### Drug Interactions

No drug interactions are reported.

### Instructions for Use

For treatment of pemphigus skin disease, it is usually administered with a tetracycline.

### Patient Monitoring and Laboratory Tests

Monitor blood CBC periodically during treatment.

### Formulations

- Niacinamide is available in 50-, 100-, 125-, 250-, and 500-mg tablets (OTC) and 100-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 500 mg niacinamide q8h PO, plus 500 mg tetracycline. This dose is approximate based on a 10-kg dog. Eventually taper dose to q12h, then to q24h. For dogs <10 kg, start with 250 mg of each drug.

## Large Animal Dosage

- No large animal doses are reported.

## Regulatory Information

No regulatory information is available. Because of the low risk of residues, no withdrawal times are suggested.

## Nifedipine

nye-fed'ih-peen

**Trade and other names:** Adalat and Procardia

**Functional classification:** Calcium-channel blocker, vasodilator

## Pharmacology and Mechanism of Action

Calcium-channel blocking drug of the dihydropyridine class. Vasodilator. The action of nifedipine is similar to other calcium-channel blocking drugs, such as amlodipine. They block voltage-dependent calcium entry into smooth muscle cells. Drugs of the dihydropyridine class are more specific for vascular smooth muscle than the cardiac tissue. Therefore they have less effect on cardiac conduction than diltiazem.

## Indications and Clinical Uses

Nifedipine is used for smooth muscle relaxation and to induce vasodilation. It is indicated for treatment of systemic hypertension. Use in animals is rare because there is more experience with amlodipine. The use of nifedipine in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects have not been reported in veterinary medicine. The most common side effect is hypotension.

### Contraindications and Precautions

Do not administer to a patient with hypotension. Nifedipine may be teratogenic in pregnant laboratory animals and/or embryotoxic. Avoid use in pregnant animals.

### Drug Interactions

Do not administer with drugs known to inhibit drug-metabolizing enzymes (e.g., ketoconazole). Nifedipine may be subject to interactions from drugs that inhibit the membrane multidrug resistance pump, also known as P-glycoprotein, which may lead to toxicity. See Appendix J for drugs that may affect P-glycoprotein.

## Instructions for Use

Use of nifedipine is limited in veterinary medicine. Other calcium-channel blockers, such as diltiazem, are used to control heart rhythm. Amlodipine is more commonly used for control of systemic hypertension.

## Patient Monitoring and Laboratory Tests

Monitor blood pressure during therapy.

## Formulations

- Nifedipine is available in 10- and 20-mg capsules and 30-, 60-, and 90-mg extended-release tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is decomposed more rapidly if exposed to light. In extemporaneous solutions, nifedipine is unstable. If mixed with solutions, it should be used immediately.

## Small Animal Dosage

- Animal dose not established. In people, the dose is 10 mg/per person three times a day and increased in 10-mg increments to effect.

## Large Animal Dosage

- No large animal doses are reported.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Nitazoxanide

nye-taz-oks'ah-nide

**Trade and other names:** Navigator (horse preparation) and Alinia (human preparation)

**Functional classification:** Antiprotozoal

## Pharmacology and Mechanism of Action

Antiprotozoal drug. Nitazoxanide (NTZ) is a nitrothiazolyl-salicylamide derivative. Its action against protozoa is unknown, but it may be related to the inhibition of the pyruvate-ferredoxin oxidoreductase (PFOR) enzyme-dependent electron transfer reaction essential to anaerobic and protozoal energy metabolism. Activity has been demonstrated against a variety of protozoa, including *Cryptosporidium parvum*, *Giardia*, *Isospora*, and *Entamoeba*. It also has activity against intestinal helminths, such as *Ascaris*, *Ancylostoma*, *Trichuris*, and *Taenia*. It also may be active against some anaerobic bacteria, including *Helicobacter*. One of the active metabolites is tizoxanide.

## Indications and Clinical Uses

Nitazoxanide was used to treat equine protozoal myeloencephalitis (EPM) as the equine paste Navigator® (32% paste). However because the adverse effects were common, and included fatal enterocolitis at recommended doses, it was voluntarily withdrawn by the sponsor. It is still available in the human formulation. It has had only limited use in other veterinary species, but there is a form approved for use in people

for treatment of protozoal infections, such as *C. parvum* and *Giardia*. There has been only limited use in dogs and cats for intestinal protozoal infections but no reports to document efficacy and safety. In people, it has been used to treat intestinal infections caused by *Cryptosporidium* (500 mg per person q12h for 3 days) with good success. There are no reports of its use to treat *Cryptosporidium* in animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Because it may disrupt normal intestinal flora, administration to some animals has produced diarrhea.

#### Contraindications and Precautions

No known contraindications.

#### Drug Interactions

No known drug interactions.

### Instructions for Use

Nitazoxanide was administered for horses to treat EPM, but the equine product has been withdrawn from the market. Use in small animals has been extrapolated from use in humans.

### Patient Monitoring and Laboratory Tests

When treating patients for diarrhea, monitor electrolytes and fecal samples.

### Formulations

- Nitazoxanide was available in a 0.32-mg/mL oral paste for horses, but has been withdrawn from the market by the sponsor. Human formulation is a powder for oral dosing; 100 mg of powder is mixed with 48 mL of water.

### Stability and Storage

Stable if stored in manufacturer's original formulation. The oral solution for people can be mixed and remain stable for 7 days.

### Small Animal Dosage

- There are no small animal dosing instructions available. However, one dose that has been used is 100 mg per animal q12h PO for 3 days.

### Large Animal Dosage

#### Horses

- 25 mg/kg q24h PO on days 1 through 5, followed by 50 mg/kg q24h PO on days 6 through 28. (The equine product was withdrawn from the market by the sponsor because of severe adverse effects.)

### Regulatory Information

Do not use in animals intended for food.

## Nitenpyram

nye-ten-pye'ram

**Trade and other names:** Capstar

**Functional classification:** Antiparasitic



## **Pharmacology and Mechanism of Action**

Nitenpyram is an antiparasitic drug used for treatment of fleas. It will rapidly kill adult fleas. It is from the class of synthetic insecticides known as the neonicotinoids. It is related to imidacloprid and has the same mechanism of action, which is to inhibit postsynaptic nicotinic acetylcholine receptors, which produces influx of sodium ions. Nitenpyram is absorbed completely from oral administration and has a half-life in dogs and cats of 2.8 and 7.7 hours, respectively. After oral absorption it produces a rapid kill of adult fleas that has been observed as quickly as 30 minutes after drug administration, and is 98.6% effective in dogs and 98.4% effective in cats.

## **Indications and Clinical Uses**

Nitenpyram is used to kill fleas on dogs and cats. It produces a rapid kill, with fleas killed within an hour of administration. It is often used with other drugs that act to prevent flea infestations as part of a comprehensive flea-control program.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

No adverse reactions are reported. It was safe in studies in dogs and cats in which up to 10 times the dose was administered. It was tolerated even in young animals even at 8 weeks of age. Some transient pruritus may occur shortly after administration, which coincides with the initial killing of fleas.

#### **Contraindications and Precautions**

Do not use in dogs or cats <1 kg (2 pounds) in weight. Do not use in cats or dogs younger than 4 weeks of age.

#### **Drug Interactions**

No drug interactions have been reported. It is safe to use with lufenuron and milbemycin.

## **Instructions for Use**

Nitenpyram is often used with lufenuron to kill adult fleas and prevent flea eggs from hatching. Administer with or without food.

## **Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

## **Formulations**

- Nitenpyram is available in 11.4- or 57-mg tablets.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

## **Small Animal Dosage**

- 1 mg/kg daily PO as needed to kill fleas.

## **Large Animal Dosage**

- No large animal dose is reported.

## **Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Nitrofurantoin

nye-troe-fyoo'ran-toyn

**Trade and other names:** Macrochantin, Furalan, Furatoin, Furadantin, and generic brands

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Antibacterial drug. Urinary antiseptic. Therapeutic concentrations are reached only in the urine. In people, these concentrations reach 200 mcg/mL, but plasma concentrations are almost undetectable. In the urine, it is reduced by bacterial flavoproteins, and the reactive metabolites bind to bacterial ribosomes and inhibit bacterial enzymes involved in the synthesis of DNA and RNA. The spectrum includes *Escherichia coli*, *Staphylococcus* spp., and *Enterococcus* spp. Resistance among bacteria is unusual, although *Proteus* and *Pseudomonas aeruginosa* are inherently resistant. Pharmacokinetics have been studied in laboratory animals and people. The macrocrystalline form is slowly absorbed and less likely to cause gastric upset. The microcrystalline form is rapidly absorbed in the intestine. In dogs, oral absorption is uncertain.

### Indications and Clinical Uses

Nitrofurantoin has been an important drug for short-term treatment of urinary tract infections in people. The use in animals is not as common, but can be considered for some cases of urinary tract infection. It is advised to use the macrocrystalline form to reduce GI upset and prolong effects. Although nitrofurantoin can be administered orally for treatment or prevention of urinary tract infections (UTIs), it does not attain high enough concentrations for other infections. Although it is used in animals for UTI, the use in animals has been primarily derived from empirical use or from experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness in veterinary medicine. There have been in vitro microbiologic studies to demonstrate activity against a broad spectrum of bacteria, including those resistant to other antimicrobials.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects include nausea, vomiting, and diarrhea. It turns urine color rust-yellow brown. In people, respiratory problems (pneumonitis) and peripheral neuropathy have been reported. The polyneuropathies in people are caused by a demyelination and are more common from long-term use or in patients with renal compromise. The respiratory problems have not been reported in animals, but neuropathy has been observed in dogs; the risk may be higher if there is renal insufficiency.

#### Contraindications and Precautions

Do not administer during pregnancy, especially at term, because it may cause hemolytic anemia of the newborn. Do not administer to neonates. Do not rely on nitrofurantoin for systemic infections, infections of the kidney or prostate. It is active against lower urinary tract infections only.

#### Drug Interactions

Do not give medications that may alkalize the urine because this may reduce effectiveness.

### Instructions for Use

Two dosing forms exist. Microcrystalline is rapidly and completely absorbed. Macrocrystalline (Macrochantin) is more slowly absorbed and causes less GI irritation. Urine should be at acidic pH for maximum effect. Administer with food to increase absorption.

### Patient Monitoring and Laboratory Tests

Monitor urine cultures and/or urinalysis. A microbiologic susceptibility test may overestimate the true activity against some bacteria.

### Formulations

- Macrochantin and generic brands are available in 25-, 50-, and 100-mg capsules (macrocrystalline) and Furalan, Furatoin, and generic brands are available in 50- and 100-mg tablets (microcrystalline). Furadantin is available in 5-mg/mL oral suspension.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is slightly soluble at a concentration less than 1 mg/mL in water and ethanol. It decomposes if exposed to metals other than stainless steel or aluminum.

### Small Animal Dosage

#### Dogs and Cats

- 10 mg/kg/day divided into four daily treatments. Then 1 mg/kg at night PO.
- Macrocrystalline formulation: 2-3 mg/kg q8h PO, followed by 1-2 mg/kg once at nighttime.

### Large Animal Dosage

#### Horses

- 2 mg/kg q8h PO.

### Regulatory Information

It is prohibited from use in animals intended for food.

## Nitroglycerin

nye-troe-glih'ser-in

**Trade and other names:** Nitrol, Nitro-bid, and Nitrostat

**Functional classification:** Vasodilator

### Pharmacology and Mechanism of Action

Nitrate. Nitrovasodilator. Like other nitrovasodilators, it relaxes vascular smooth muscle (especially venous) via generation of nitric oxide (NO). The nitrate vasodilators are esters of nitrous acid. They are metabolized to inorganic nitrite and denitrated metabolites. Nitrites, organic nitrates, and nitroso compounds all act to activate the enzyme guanylate cyclase, which in turn produces cyclic guanosine monophosphate (GMP) in vascular smooth muscle and relax smooth muscle. Nitric oxide is also known as the endothelium-derived relaxing factor (EDRF).

Nitric oxide-generating compounds may also help decrease gastric adverse effects associated with NSAIDs. Plasma concentrations are attained within 2 minutes, but the half-life in animals is short (only 1-3 minutes) with high first-pass effects (i.e., not absorbed from oral administration).

## Indications and Clinical Uses

Nitroglycerin, like other nitrovasodilators, is used primarily in heart failure or pulmonary edema to reduce preload or decrease pulmonary hypertension. Nitrates relax smooth muscle in both arteries and veins, but they are often used clinically as preload reducers. When used as preload reducers, they decrease myocardial O<sub>2</sub> requirements (decrease workload of heart). Because of this effect, they have been commonly used to manage human patients with angina pectoris (chest pain caused by cardiovascular disease).

Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. In horses, nitroglycerin has been used to improve blood flow to the feet in the management of laminitis. However, in experiments, this treatment was not effective in horses and did not increase blood flow to the feet.

### Precautionary Information

#### Adverse Reactions and Side Effects

The most significant adverse effect is hypotension. Methemoglobinemia can occur with accumulation of nitrites, but it is a rare problem.

#### Contraindications and Precautions

Do not administer to patients with hypotension. Warn pet owners not to apply ointment without wearing gloves.

#### Drug Interactions

No drug interactions are reported for animals.

## Instructions for Use

Tolerance can develop with repeated chronic use. Tolerance may be caused by a progressive depletion of sulfhydryl groups necessary for the formation of NO. Efficacy is improved if the drug is used intermittently instead of continuously because intermittent use allows time for regeneration of sulfhydryl groups. Optimum intermittent use is to provide a nitrate-free interval of 8 hours or more during the day. Nitroglycerin has high presystemic metabolism, and oral availability is poor. When using ointment, 1 inch of ointment is approximately 15 mg.

It is usually applied to an area on the patient that lacks hair and where the patient will not lick it off (such as pinnae of ears).

## Patient Monitoring and Laboratory Tests

Monitor patient's blood pressure during therapy.

## Formulations

- Nitroglycerin is available in 0.5-, 0.8-, 1-, 5-, and 10-mg/mL injection; 2% ointment, 0.3-, 0.4-, and 0.6-mg sublingual tablets; translingual spray; and transdermal systems (0.2 mg/hr patch).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Nitroglycerin tablets are very heat and light sensitive and should be stored in a tightly sealed glass bottle.

## Small Animal Dosage

### Dogs

- 4-12 mg (up to 15 mg) topically as needed. In dogs, it has been used as one-fourths to three-fourths inch of 2% ointment every 6 hr (1 inch equals 15 mg).

## 570 Nitroprusside (Sodium Nitroprusside)

### Cats

- 2-4 mg topically, or typically one-eighth to one-quarter inch every 4-6 hr.

### Large Animal Dosage

#### Horses

- Treatment of laminitis: Apply 2% ointment to skin above hoof (efficacy questionable).

### Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 3

## Nitroprusside (Sodium Nitroprusside)

nye-troe-pruss'ide

**Trade and other names:** Nitropress

**Functional classification:** Vasodilator

### Pharmacology and Mechanism of Action

Nitrate vasodilator. Like other nitrovasodilators, it relaxes vascular smooth muscle (especially venous) via generation of NO. Nitric oxide stimulates guanylate cyclase to produce GMP in smooth muscle, with a predominant effect of relaxing vascular smooth muscle. Nitroprusside is used only as an IV infusion, and patients should be monitored carefully during administration. Nitroprusside has a rapid onset of effect (almost immediately) and a duration that lasts only minutes after discontinuation of IV administration.

### Indications and Clinical Uses

Nitroprusside is used for acute management of pulmonary edema and other hypertensive conditions. It is administered only by IV infusion, and the dose is titrated carefully by monitoring systemic blood pressure. Titrate to maintain the arterial blood pressure to 70 mm Hg. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

Severe hypotension is possible during therapy. Reflex tachycardia can occur during treatment. Cyanide is generated via metabolism during nitroprusside treatment, especially at high infusion rates ( $>5$  mcg/kg/min). At high infusion rates ( $>10$  mcg/kg/min), seizures may occur, which are signs of cyanide toxicity. Sodium thiosulfate has been used in people to prevent cyanide toxicity. Methemoglobinemia is possible and, if necessary, treated with methylene blue.

#### Contraindications and Precautions

Do not administer to patients with hypotension or who are dehydrated.

#### Drug Interactions

No drug interactions are reported for animals.

### Instructions for Use

Nitroprusside is administered via IV infusion. Intravenous solution should be delivered in 5% dextrose solution. (For example, add 20-50 mg to 250 mL of 5% dextrose to a

concentration of 80 to 200 mcg/mL.) Protect from light with opaque wrapping. Discard solutions if color change is observed. Titrate dose carefully in each patient.

### Patient Monitoring and Laboratory Tests

Monitor blood pressure carefully during administration. Do not allow blood pressure to fall below 70 mm Hg during treatment. Monitor heart rate because reflex tachycardia is possible during infusion.

### Formulations Available

- Nitroprusside is available in a 50-mg vial for injection at 10 and 25 mg/mL.

### Stability and Storage

Not compatible in some fluids. For IV use, dilute with 5% dextrose. Protect from light and cover infusion solution during administration. Nitroprusside decomposes quickly in alkaline solutions or with exposure to light.

### Small Animal Dosage

#### Dogs and Cats

- 1-5 mcg/kg/min IV, up to a maximum of 10 mcg/kg/min. Generally, start with 2 mcg/kg/min and increase gradually by 1 mcg/kg/min until desired blood pressure is achieved.

### Large Animal Dosage

- No large animal doses are reported.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

N

## Nizatidine

nih-zah'tih-deen

**Trade and other names:** Axid

**Functional classification:** Antiulcer agent

### Pharmacology and Mechanism of Action

Histamine H<sub>2</sub>-blocking drug. Nizatidine blocks histamine stimulation of gastric parietal cells to decrease gastric acid secretion. It is 4 to 10 times more potent than cimetidine. Nizatidine and ranitidine also have been shown to stimulate gastric emptying and colonic motility via anticholinesterase activity. It is also used to treat gastric ulcers and gastritis.

### Indications and Clinical Uses

Nizatidine, like other H<sub>2</sub>-receptor blockers, is used to treat ulcers and gastritis. These drugs inhibit secretion of stomach acid and have also been used to prevent ulcers caused from NSAIDs, but the efficacy for this use has not been demonstrated. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. In animals, famotidine or ranitidine is used more commonly as an H<sub>2</sub>-receptor blocker, or omeprazole is used as a proton pump inhibitor (PPI).

**Precautionary Information****Adverse Reactions and Side Effects**

Side effects from nizatidine have not been reported for animals.

**Contraindications and Precautions**

No contraindications have been reported for animals.

**Drug Interactions**

No drug interactions are reported for animals.

**Instructions for Use**

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Nizatidine use in animals has not been as common as the use of other related drugs such as ranitidine or famotidine.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Nizatidine is available in 150- and 300-mg capsules and 15-mg/mL oral solution

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Nizatidine is slightly soluble in water. It has been mixed with juices and syrups for oral administration and was stable for 48 hours. Avoid mixing with Maalox liquid.

**Small Animal Dosage****Dogs**

- 2.5-5 mg/kg q24h PO.

**Large Animal Dosage**

- No large animal doses are reported.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).  
RCI Classification: 5

**Norfloxacin**

nor-floks'ah-sin

**Trade and other names:** Noroxin

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Fluoroquinolone antibacterial drug. Norfloxacin acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. It is a bactericidal with a broad spectrum of activity. Sensitive bacteria include *Staphylococcus*, *Escherichia coli*, *Proteus*, *Klebsiella*, and *Pasteurella*. *Pseudomonas aeruginosa* is moderately sensitive. However, norfloxacin is not as active as other drugs in the fluoroquinolone group.

## Indications and Clinical Uses

Norfloxacin has been replaced by other veterinary fluoroquinolones because they have more favorable pharmacokinetics and improved spectrum of activity. However, it has been used to treat a variety of infections, including respiratory, urinary tract, skin, and soft tissue infections.

### Precautionary Information

#### Adverse Reactions and Side Effects

High concentrations may cause central nervous system (CNS) toxicity, especially in animals with renal failure. Norfloxacin may cause some nausea, vomiting, and diarrhea at high doses. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4 to 28 weeks of age. Large, rapidly growing dogs are the most susceptible.

#### Contraindications and Precautions

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures. Norfloxacin may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), may decrease absorption.

#### Drug Interactions

No drug interactions are reported for animals. However, like other quinolones, coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

## Instructions for Use

Use in animals (and doses) is based on pharmacokinetic studies in experimental animals, experience in people, or anecdotal experience in animals.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) breakpoints for sensitive organisms are less than or equal to 4 mcg/mL.

## Formulations

- Norfloxacin is available in 400-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- 22 mg/kg q12h PO.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

It is prohibited from use in animals intended for food.



## Oclacitinib Maleate

(ok'la sye'ti nib mal'ee ate)

**Trade and other names:** Apoquel

**Functional Classification:** Anti-inflammatory, Antipruritic

### Pharmacology and Mechanism of Action

Oclacitinib is a Janus kinase (JAK) inhibitor used for control of pruritus in dogs associated with allergic dermatitis and atopic dermatitis. Oclacitinib has a unique mechanism of action that acts to inhibit proinflammatory cytokines. It inhibits cytokines involved with pruritus in dogs that are dependent on the JAK enzyme. It inhibits preferentially the JAK1 enzyme activity over JAK2 or JAK3, with a 1.8-fold selectivity over JAK2 and 9.9-fold selectivity over JAK3. This preferential activity is important because JAK2 is involved with hematopoiesis and high doses of oclacitinib could suppress hematopoiesis. Of significance for atopic and allergic dermatitis treatment is that oclacitinib inhibits the IL-31 cytokine function and reduces IL-31 induced pruritus in dogs. It also may inhibit the function of other proinflammatory cytokines such as IL-2, IL-4, IL-6, and IL-13 that may be involved with allergy.

In studies of dogs with atopic dermatitis, the efficacy was 66% and 49% as assessed by pet owners and veterinarians, respectively, and 67% in a study with allergic dermatitis. This was significantly better than placebo. Oclacitinib also was shown to have equal efficacy as prednisolone in dogs, with an onset of efficacy of both treatments in as little as 4 hours.

Oclacitinib is rapidly absorbed (89% bioavailability) and reaches a peak in less than 1 hour, producing rapid effects after administration. The rapid onset of action distinguishes it from some of the other products currently used for treatment of this disease. After absorption, the half-life is approximately 3-5 hours in dogs. Pharmacokinetics are not affected by feeding or breed of dog. The predominant clearance route is hepatic with small amounts of renal and biliary elimination.

### Indications and Clinical Use

Oclacitinib is indicated for control of pruritus associated with allergic dermatitis and control of atopic dermatitis in dogs at least 12 months of age.

*Use in cats:* The clinical use in cats has not been limited to some isolated case reports. At a dose of 0.4-0.6 mg/kg twice daily for 14 days, then tapered to once-daily in small numbers of cats it has produced good to excellent results. The dose examined in some experimental cats has been approximately 0.5 mg/kg every 12 hours. There may be a potential role for oclacitinib and other JAK inhibitors for treatment of feline asthma and allergic dermatitis, but further studies are necessary to establish clinical use.

### Precautionary Information

#### Adverse Effects

During field studies there was a low rate of adverse reactions (diarrhea, 2.3%-4.6% and vomiting, 2.3%-3.9%), which were not different from the placebo and usually resolved after initial dosing. In a clinical study there was a 9.2% incidence of vomiting and 6% incidence of diarrhea in 283 dogs. Treated dogs had decreased leukocytes and serum globulin compared to placebo group. In field trials there have been isolated cases of demodicosis, pyoderma, pneumonia, and mast cell tumor or other neoplasms, but it is not known if these were associated with the medication.

If administration is continued at twice daily, compared with once daily, more adverse effects may be anticipated. There was a mild, dose-dependent reduction in

hemoglobin, hematocrit, and reticulocyte counts during the twice-daily dosing period for 60 days with decreases in the leukocyte subsets of lymphocytes, eosinophils, and basophils. High doses can potentially cause impairment of immune surveillance against tumors; therefore, high doses should be avoided.

### Contraindications and Precautions

Safety has not been evaluated in breeding animals or during pregnancy. The manufacturer warns that oclacitinib should not be administered to dogs less than 12 months of age or dogs with serious infections. Oclacitinib may increase susceptibility to infection, including demodicosis, and exacerbate neoplastic conditions.

*Vaccination:* At an oclacitinib dose that represented three times the therapeutic dose, dogs mounted an adequate immune response to killed rabies, modified live canine distemper virus, and modified live canine parvovirus vaccination in 16-week-old vaccine-naïve dogs. Approximately 80% of the dogs had adequate response to canine parainfluenza virus.

### Drug Interactions

Dermatologists have used oclacitinib with other medications such as corticosteroids, cyclosporine, and other systemic agents safely, but the manufacturer warns that safety with these medications has not been evaluated. Inhibition of canine cytochrome P450 enzymes by oclacitinib is minimal with the inhibitor concentrations 50 times higher than the peak concentrations produced from the therapeutic dose.

### Patient Monitoring

No specific monitoring is necessary. If doses are continued at a twice-daily schedule for longer than the manufacturer recommends, monitor complete blood count (CBC) periodically to assess effects on bone marrow.

### Instructions for Use

Oclacitinib is indicated for dogs only, and safe doses have not been established in other animals. It should not be administered to humans. Administer according to the sponsor's instructions. After the initial induction period of twice-daily dosing, it should be reduced to once-daily administration to decrease risk of adverse effects. According to the manufacturer's information, a dose of 0.4-0.6 mg twice daily was initially proposed for long-term use. However, there were questions of safety with the long-term twice-daily dose and concerns because immunosuppression, including bacterial pneumonia and infections caused by *Demodex*, were observed in the high dose (three times and five times) treatment groups with twice-daily administration.

### Formulations

- Oclacitinib is available as a 3.6-, 5.4-, or 16-mg tablet. Do not use compounded formulations because stability and potency have not been evaluated.

### Storage Conditions

Store at room temperature between 20° and 25° C (68° and 77° F) in manufacturer-recommended container. The pH can affect solubility. At pH 4 it is less soluble and at pH 5.5 it is almost completely insoluble.

### Small Animal Dosage

- Dogs: 0.5 mg/kg (0.4-0.6 mg/kg, with or without food) initially on a twice-daily schedule for the first 14 days, then tapered to a once-daily administration.
- Cats: Dose has not been established for cats.

**Large Animal Dosage**

- No large animal doses have been established.

**Regulatory Information**

No regulatory information is available. Oclacitinib should not be administered to animals intended for food.

**Olsalazine Sodium**

ole-sal'ah-zeen soe'dee-um

**Trade and other names:** Dipentum

**Functional classification:** Antidiarrheal

**Pharmacology and Mechanism of Action**

Anti-inflammatory drug composed of two molecules of aminosalicic acid joined by an azo bond. Each component is released in the colon by bacterial enzymes. The released drug is also known as mesalamine (see separate entry for mesalamine). Mesalamine is also the active component of sulfasalazine, which is commonly administered for treatment of colitis. The action of mesalamine is not precisely known, but it appears to suppress the metabolism of arachidonic acid in the intestine. It inhibits both cyclooxygenase- and lipoxygenase-mediated mucosal inflammation. Systemic absorption is small; most of the action is believed to be local. Olsalazine has a similar effect as sulfasalazine but without the sulfonamide component. Other formulations of mesalamine include Asacol, Mesasal, and Pentasa. The others are coated tablets designed to release the active component in the intestine.

**Indications and Clinical Uses**

Olsalazine, like other forms of mesalamine, is used for treatment of inflammatory bowel disease, including colitis in animals. In small animals, most often sulfasalazine is used; however, in some animals olsalazine may be indicated. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

**Precautionary Information****Adverse Reactions and Side Effects**

No adverse effects reported in animals.

**Contraindications and Precautions**

Do not administer to patients sensitive to salicylate compounds.

**Drug Interactions**

No drug interactions have been reported for animals.

**Instructions for Use**

Olsalazine is used in patients that cannot tolerate sulfasalazine.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Olsalazine is available in 500-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

- Dose not established, but 5-10 mg/kg q8h have been used. (The usual human dose is 500 mg twice daily.)

### Large Animal Dosage

- No doses are reported for large animals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

Racing Commissioners International (RCI) Classification: 4

## Omeprazole

oh-mep'rah-zole

**Trade and other names:** Prilosec (formerly Losec; human preparation), Zegerid (human formulation), GastroGard, and UlcerGard (equine preparations), outside the United States Peptizole and Gastrozol are available for horses.

**Functional classification:** Antiulcer agent

### Pharmacology and Mechanism of Action

Proton pump inhibitor (PPI). Omeprazole inhibits gastric acid secretion by inhibiting the  $K^+/H^+$  pump (potassium pump). Omeprazole is more potent and longer acting than most available antisecretory drugs. Other PPIs include pantoprazole (Protonix), lansoprazole (Prevacid), and rabeprazole (Aciphex). They all act via similar mechanism and are equally effective. Proton pump inhibitors also have some effect for inhibiting *Helicobacter* organisms in the stomach when administered with antibiotics. Omeprazole is decomposed in the acid environment of the stomach. Oral absorption is decreased if administered with food. Formulations are designed to protect from acid—such as with a buffering added or enteric coating—to improve oral absorption. Some human formulations also contain bicarbonate. When administered orally to horses, maximum serum concentration occurs at 45-60 minutes with effective acid suppression within 1-2 hours. Half-life from oral administration to horses varies from 70-100 minutes, depending on the formulation. Pharmacokinetics and acid suppression have also been studied in dogs and cats, with effective acid suppression at the dosages provided in the dosing section. An equivalent drug is esomeprazole (Nexium), which is the S-isomer of omeprazole (the active isomer). It is expected to have equal efficacy at equivalent dosages.

### Indications and Clinical Uses

Omeprazole, like other PPIs, is used for treatment and prevention of gastrointestinal ulcers. It has been used in dogs, cats, and exotic species, but most efficacy data for animals have been produced in horses, in which it has been shown that omeprazole is effective for treating and preventing gastric ulcers. In foals, 4 mg/kg q24h suppressed acid secretion for 22 hours. By comparison, ranitidine suppressed acid up to 8 hours at a dose of 6.6 mg/kg. In studies performed in horses, omeprazole was more effective than ranitidine for treating gastric ulcers. For treatment of ulcers in horses, the approved label treatment in the US is 4 mg/kg oral, once per day. However, there is evidence to indicate that a dose of 1 mg/kg per day is equally effective. Response is generally better for squamous ulceration in horses than glandular ulceration. Effects were observed within 14 days, but recurrence was observed after treatment was discontinued.

The equine formulations in the US (GastroGard and UlcerGard) are buffered formulations. An enteric-coated formulation is available for horses in some countries (Gastrozol). Both formulations, when combined with environmental changes, promote healing of gastric ulcers in horses. Plasma omeprazole concentrations after single doses were significantly higher with GastroGard than Gastrozol when each was administered at the labeled dose.

In dogs, 1 mg/kg q24h PO is as effective as pantoprazole (1 mg/kg) and famotidine (0.5 mg/kg q12h) for maintaining stomach pH >3-4. Repeated doses may be necessary (two to five doses) for complete inhibition of acid secretion. In dogs and cats, PPIs may be more effective than other drugs (e.g., histamine H<sub>2</sub> blockers) because of the long duration of effect. In cats, the equine formulation (listed later) and fractionated tablets were equally effective for suppressing acid secretion and were superior to an H<sub>2</sub>-blocker (famotidine). In a similar study performed in dogs, omeprazole tablets or equine paste administered once daily provided superior acid suppression compared to famotidine twice daily.

Omeprazole, like other PPIs, may be effective for preventing nonsteroidal anti-inflammatory drug (NSAID)-induced ulcers. Omeprazole has also been used in combination with other drugs (antibiotics) for treatment of *Helicobacter* infections in animals.

## **Precautionary Information**

### **Adverse Reactions and Side Effects**

The only reported adverse effect in dogs has been diarrhea in some cases. Otherwise, adverse effects have not been reported in animals. However, in people there is concern about hypergastrinemia with chronic use. Horses have tolerated 20 mg/kg q24h for 91 days and 40 mg/kg q24h PO for 21 days. Dogs and cats also have tolerated the regimens listed in the dosing section. Overgrowth of *Clostridium* bacteria has been a concern from chronic use because of chronic gastric acid suppression, but the clinical importance of this concern in animals has not been established. In people, long-term use of PPIs has been associated with a modest risk of hip fractures because of decreased oral absorption of calcium and increased bone resorption by osteoclasts. This problem has not been reported in animals.

### **Contraindications and Precautions**

One of the human formulations (Zegerid) is a packet to be mixed with water for oral administration. This formulation contains xylitol, which can be toxic to dogs if administered at high doses or with other medications that contain xylitol.

### **Drug Interactions**

Although omeprazole has not been associated with drug interactions in animals, PPIs may inhibit some drug-metabolizing enzymes (CYP450 enzymes). In people, metabolism of clopidogrel to the active metabolite can be inhibited by omeprazole, but this inhibition was not demonstrated in studies in dogs and has not been studied in horses or cats. Metabolism of other drugs may be inhibited by omeprazole, but this has not been studied in domestic animals. Because of stomach acid suppression, do not administer with drugs that depend on stomach acid for absorption (e.g., ketoconazole and itraconazole). In people there may be an increased risk of intestinal injury when proton pump inhibitors are administered with NSAIDs, but this has not been studied in animals.

## **Instructions for Use**

Omeprazole is the most common drug of this class used in animals. Other PPIs include pantoprazole (Protonix), lansoprazole (Prevacid), and rabeprazole (Aciphex).

No experience with these other products is reported for veterinary medicine. In people, they are all considered equally efficacious. Pantoprazole and rabeprazole have the advantage in that they are available as tablets that can be crushed.

The equine formulations available include GastroGard and UlcerGard, which are buffered formulations to enhance oral absorption. Gastrozol is an enteric-coated formulation for horses available in Australia (see “[Indications and Clinical Use](#)” section for comparison). Rectal administration has been studied in horses but has produced low and inconsistent response. Because there are no small animal formulations available, the human forms have been administered to dogs and cats, and the equine formulation has been diluted in oil to 40 mg/mL for administration to small animals. Preliminary studies have shown that the equine formulation administered orally to dogs can be efficacious.

### Patient Monitoring and Laboratory Tests

Omeprazole and PPIs are generally considered safe. No routine tests for monitoring adverse effects are recommended. If gastrin concentrations are measured, a 7-day withdrawal from omeprazole treatment should be used; otherwise, there is a significant increase in serum gastrin concentrations from omeprazole treatment.

### Formulations

- Omeprazole is available in 20-mg capsules (human preparation) and in an equine paste, GastroGard. The over-the-counter (OTC) equine paste is UlcerGard. Paste for horses is 370 mg/gram of paste in a buffered formulation to prevent degradation in the stomach. Gastrozol is a enteric-coated formulation in a paste available in Australia for horses, but is not approved in the US. A human oral formulation (Zegerid) is available either as 40-mg or 20-mg capsules with 1100 mg sodium bicarbonate. Zegerid is also available either as 40-mg or 20-mg single-dose packets of powder for oral suspension with 1680 mg sodium bicarbonate.
- *Compounded formulations:* Compounded formulations must be produced from a Food and Drug Administration (FDA)–finished formulation. Studies using compounded products from non-FDA formulations in horses failed to produce therapeutic effects. Compounded formulations for dogs and cats are discussed below.

### Stability and Storage

Omeprazole should be maintained in the manufacturer’s original formulation (capsules or paste) for optimum stability and effectiveness. It is stable at pH 11 but rapidly decomposes at pH <7.8. No small animal formulations are available, and either the human formulation or equine formulation has been administered to small animals. The equine formulation can be diluted in corn oil for small animal use because it is very concentrated. It has been diluted to 10 and 40 mg/mL by suspending the approved equine oral paste formulation in oil at a ratio of 1:9 and stored at controlled cold temperature (7° C) and protected from light. The formulation has been stable for 6 months. Intravenous forms of omeprazole have been formulated in sterile water and administered to experimental horses, but these formulations are not commercially available. Studies conducted on compounded oral equine formulations have shown that these formulations have low potency.

### Small Animal Dosage

#### Dogs

- 20 mg per dog q24h PO or 1-2 mg/kg q24h PO.

#### Cats

- 1 mg/kg q24h PO.

## Large Animal Dosage

### Horses

- Treating ulcers: 4 mg/kg once daily for 4 weeks PO. There is some evidence that 1-2 mg/kg per day is as effective for treatment as a higher dose. Based on an approved formulation in some countries (Gastrozol), it was effective at the labeled dose of 1 mg/kg.
- Preventing ulcers: 1-2 mg/kg q24h PO. (1 mg/kg was effective for prevention in studies performed in horses.)
- Intravenous use (if a formulation is available): Loading dose of 1 mg/kg, followed by 0.5 mg/kg per day for 14-28 days.

### Ruminants

- Oral absorption may not be high enough for effective therapy.

## Regulatory Information

Not intended for administration to animals that produce food. Oral absorption in ruminants is not established. Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 5

## Ondansetron Hydrochloride

on-dan'sih-tron hye-droe-klor'ide

**Trade and other names:** Zofran

**Functional classification:** Antiemetic

## Pharmacology and Mechanism of Action

Ondansetron is an antiemetic drug from the class of drugs called *serotonin antagonists*. Like other drugs of this class, ondansetron acts by inhibiting serotonin type 3 (5-HT<sub>3</sub>) receptors. It is effective as an antiemetic during chemotherapy, for which it has been effective by blocking emetic stimuli that release serotonin. During chemotherapy or following gastrointestinal injury, there may be 5-HT released from the gastrointestinal tract that stimulates vomiting centrally. This stimulus is blocked by this class of drugs. These drugs also have been used to treat vomiting from other forms of gastroenteritis, pancreatitis, and inflammatory bowel disease. In cats, the oral absorption was 32% from oral administration and 75% from subcutaneous administration. The half-life in cats was 1.8 hours from IV administration, 1.2 hours from oral administration, and more prolonged (3.2 hours) from subcutaneous administration. In dogs, it is much less bioavailable (<10%) after oral administration and has a shorter half-life of 30 minutes, raising questions about the clinical effectiveness of ondansetron in dogs.

Other serotonin antagonists used for antiemetic therapy include granisetron, ondansetron, dolasetron, azasetron, and tropisetron.

## Indications and Clinical Uses

Ondansetron, like other serotonin antagonists, is used to prevent vomiting. It can be effective for various types of vomiting that originate from injury to the gastrointestinal tract. It is effective to prevent vomiting from drug chemotherapy (cancer drugs and

dexmedetomidine). Only limited efficacy information is available for ondansetron effectiveness in animals, but oncologists have found it to be effective for managing vomiting from chemotherapy in animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Ondansetron adverse effects have not been reported in animals. These drugs have little affinity for other 5-HT receptors. Because some severe adverse effects can occur from concurrent cancer drugs, it may be difficult to distinguish these from ondansetron effects.

#### Contraindications and Precautions

There are no important contraindications identified in animals. Because it is eliminated via metabolism, it is unlikely that dose modifications are needed in animals with kidney impairment.

#### Drug Interactions

If infused through an IV catheter, it may precipitate if mixed with other drugs (e.g., metoclopramide). Other drug interactions have not been reported for animals.

### Instructions for Use

Ondansetron has been used in dogs and cats. Based on pharmacokinetic studies, it may be unlikely to maintain effective concentrations at a dose of 0.5 mg/kg q12h orally or IV, but because of a longer subcutaneous half-life, may be better suited for administration via this route. In dogs, the oral absorption is low (less than 10%) because of high first-pass metabolism and a short-half-life, which raises questions about effectiveness at doses that have been recommended but not tested for efficacy. Granisetron is a similar drug that has been substituted for a similar purpose.

### Patient Monitoring and Laboratory Tests

Monitor gastrointestinal signs in a vomiting patient.

### Formulations

- Ondansetron is available in 4- and 8-mg tablets, 4-mg/5-mL flavored syrup, and 2-mg/mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ondansetron is soluble in water. Solutions are stable, but pH should be <6 to prevent precipitation. Oral preparations have been mixed with syrups, juices, and other oral vehicles (e.g., Ora Sweet). It was stable for 42 days as long as pH remained low.

### Small Animal Dosage

#### Dogs

- 0.5-1 mg/kg 30 min prior to administration of cancer drugs intravenously. Vomiting from other causes: 0.1-0.2 mg/kg slow IV injection and repeated q6-12h. If this dose is initially ineffective, it may be increased to 0.5 mg/kg. These doses can also be administered PO, but oral absorption is low in dogs (<10%), which may compromise the effectiveness.

#### Cats

- Similar doses as dogs have been administered, or 0.5 mg/kg q12h SQ, IV, or PO. A dose of 2 mg per cat PO is common (half a tablet).



**Large Animal Dosage**

- No dosing information is available.

**Regulatory Information**

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

**Orbifloxacin**

or-bih-floks'ah sin

**Trade and other names:** Orbox

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Fluoroquinolone antimicrobial. Orbifloxacin acts via inhibition of DNA gyrase in bacteria to inhibit DNA and RNA synthesis. It is a bactericidal with a broad spectrum of activity. Spectrum includes staphylococci, gram-negative bacilli, and some *Pseudomonas* species. In dogs, the half-life is 5.6 hours; in cats, the half-life is 5.5 hours. In both species, the oral absorption is nearly 100%. However, oral suspension absorption is not as high as tablets (see “[Instructions for Use](#)” section later). In horses, it has a half-life of 5 hours and oral absorption of 68%.

**Indications and Clinical Uses**

Orbifloxacin is approved for use in dogs and cats. Like other fluoroquinolones, it is used to treat susceptible bacteria in a variety of species. Treatment of infections has included skin, soft tissue, and urinary tract infections (UTIs) in dogs and cats and soft tissue infections in horses.

**Precautionary Information****Adverse Reactions and Side Effects**

High concentrations may cause central nervous system (CNS) toxicity, especially in animals with kidney disease. It may cause some nausea, vomiting, and diarrhea at high doses. All of the fluoroquinolones may cause arthropathy in young animals. Dogs are most sensitive at 4-28 weeks of age. Large, rapidly growing dogs are the most susceptible. Blindness in cats has been reported from administration of some quinolones (nalidixic acid and enrofloxacin), but at doses up to 15 mg/kg (higher than approved label dose), orbifloxacin has not produced this effect.

**Contraindications and Precautions**

Avoid use in young animals because of risk of cartilage injury. Use cautiously in animals that may be prone to seizures.

**Drug Interactions**

Fluoroquinolones may increase concentrations of theophylline if used concurrently. Coadministration with divalent and trivalent cations, such as products containing aluminum (e.g., sucralfate), iron, and calcium, may decrease absorption. Do not mix in solutions or in vials with aluminum, calcium, iron, or zinc because chelation may occur.

## Instructions for Use

At the approved label dose, orbifloxacin is active against most susceptible bacteria. Within the approved dose range, higher doses are needed for organisms with higher minimum inhibitory concentration (MIC) values. In the cat, orbifloxacin oral suspension and orbifloxacin tablets are not bioequivalent. On a mg/kg basis, orbifloxacin oral suspension provides lower and more variable plasma levels of orbifloxacin than the tablets. The dose of orbifloxacin oral suspension in the cat is 7.5 mg/kg of body weight administered once daily, but the tablet dose can be lower. The oral suspension has been designed for palatability with an ion-exchange agent that masks the taste until it reaches the pH of the stomach.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) break point for susceptible organisms is  $\leq 1$  mcg/mL. Other fluoroquinolones may be used in some cases to estimate susceptibility to this fluoroquinolone. However, other drugs may have lower MIC values for *Pseudomonas aeruginosa*.

## Formulations

- Orbifloxacin is available in 5.7-, 22.7-, and 68-mg tablets. Oral suspension (malt flavor) is 30 mg/mL.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Orbifloxacin is slightly water soluble. It has been mixed with various syrups, flavorings, and vehicles and was stable at room temperature for 7 days. Do not mix with vehicles that contain aluminum, calcium, or iron because this may decrease oral absorption via chelation.

## Small Animal Dosage

### Dogs and Cats

- Tablets: 2.5-7.5 mg/kg q24h PO.
- Suspension in cats: 7.5 mg/kg (1 mL per kg) q24h PO.
- Suspension in dogs: 2.5-7.5 mg/kg q24h PO.

## Large Animal Dosage

### Horses

- 5 mg/kg q24h PO.

## Regulatory Information

Do not use fluoroquinolones off-label to animals that produce food. Orbifloxacin is prohibited from use in animals intended for food.

## Ormetoprim + Sulfadimethoxine

or-met'oe-prim + sul-fa-dye-meth-oks'een

**Trade and other names:** Primor

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Antibacterial drug. Ormetoprim combined with sulfadimethoxine is a synergistic combination similar to trimethoprim and sulfonamide combinations. Ormetoprim

## 584 Ormetoprim + Sulfadimethoxine

inhibits bacterial dihydrofolate reductase, and sulfonamide competes with para-aminobenzoic acid (PABA) for synthesis of nucleic acids. It can produce both bactericidal and bacteriostatic activity, depending on the organism. It has a broad antibacterial spectrum that includes common gram-positive and gram-negative bacteria. It also is active against some *Coccidia* species.

### Indications and Clinical Uses

Ormetoprim combined with sulfadimethoxine is used in small animals to treat a variety of bacterial infections caused by susceptible organisms, including pneumonia, skin, soft tissue, and UTIs in dogs and cats. In horses, it may be administered orally for infections caused by susceptible gram-positive bacteria (*Actinomyces*, *Streptococcus* spp., and *Staphylococcus* spp.), but higher doses may be needed for gram-negative infections.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, type II and III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other, more toxic metabolites may persist. Ormetoprim has been associated with some CNS effects in dogs, which include behavioral changes, anxiety, muscle tremors, and seizures. In horses, when IV doses were administered to experimental horses (IV formulation not commercially available), nervous system reactions such as tremors and muscle fasciculations were observed.

#### Contraindications and Precautions

Do not administer to animals sensitive to sulfonamides.

#### Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine.

### Instructions for Use

Doses listed are based on manufacturer's recommendations. Controlled trials have demonstrated efficacy for treatment of pyoderma on a once-daily schedule.

### Patient Monitoring and Laboratory Tests

Monitor tear production with long-term use. For susceptibility testing, break point ranges have not been determined for ormetoprim/sulfadimethoxine combinations. Use a test for trimethoprim/sulfamethoxazole combinations as a guide for susceptibility to ormetoprim/sulfadimethoxine combinations. CLSI break point for susceptible organisms is  $\leq 2/38$  mcg/mL (trimethoprim + sulfonamide).

### Formulations

- Ormetoprim/sulfadimethoxine combination is available in 120-, 240-, 600-, and 1200-mg tablets in a 5:1 ratio of sulfadimethoxine:ormetoprim.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 55 mg/kg on first day, followed by 27.5 mg/kg q24h PO. Doses can be divided into twice-daily treatments. (All doses are based on the combined milligram amount of both ormetoprim and sulfadimethoxine.)

### Cats

- Although doses are not reported by the manufacturer, doses similar to those for dogs have been administered.

## Large Animal Dosage

### Horses

- Loading dose of 55 mg/kg (of the combined drugs) followed by 27.5 mg/kg (of the combined drugs) q24h PO.

## Regulatory Information

Withdrawal times are not established for animals that produce food. Oral absorption has not been established for ruminants. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Oxacillin Sodium

oks-ah-sill'in soe'dee-um

**Trade and other names:** Prostaphlin and generic brands

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Oxacillin, like other beta-lactam antibiotics, binds penicillin-binding proteins (PBPs) that weaken or interfere with cell wall formation. After binding to PBPs, the cell wall weakens or undergoes lysis. Like other beta-lactams, this drug acts in a time-dependent manner (i.e., it is more effective when drug concentrations are maintained above the MIC during the dose interval). Oxacillin has a limited spectrum of activity that includes primarily gram-positive bacteria. Resistance is common, especially among enteric gram-negative bacilli. *Staphylococci* are susceptible because oxacillin is resistant to the bacterial beta-lactamase produced by *Staphylococcus* spp. Limited pharmacokinetic data are available for animals. Because of a short half-life and low oral absorption, there are limitations to its use in animals.

Oxacillin is not valuable therapeutically, but is used as a marker to test for *mecA*-mediated resistance of PBP2a in *Staphylococcus*. Methicillin-resistant *Staphylococcus* (e.g., MRSA or MRSP) are usually identified by using oxacillin break points (see “Patient Monitoring and Laboratory Tests” section).

## Indications and Clinical Uses

Oxacillin has had limited use in small animals for treating soft tissue infections caused by gram-positive bacteria. The most common use has been for pyoderma in dogs. Use has diminished because of limited pharmacokinetic information to guide oral dosing and the increased availability of other drugs, such as oral cephalosporins and amoxicillin and clavulanate combination.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects of penicillin-like drugs are most commonly caused by drug allergy. This can range from acute anaphylaxis when administered or other signs of allergic reaction when other routes are used. When administered orally, diarrhea is possible, especially with high doses.

### Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs.

### Drug Interactions

No drug interactions are reported. Food may inhibit oral absorption.

## Instructions for Use

Doses are based on empiricism or extrapolation from human studies. No clinical efficacy studies are available for dogs or cats. Administer on an empty stomach if possible.

## Patient Monitoring and Laboratory Tests

Culture and sensitivity testing: CLSI break points to define *mec-A*-mediated resistance in *Staphylococcus aureus* is a MIC  $\geq 4$  mcg/mL, and the zone size is  $\leq 10$  mm. All other *Staphylococcus* spp. with *mec-A*-mediated resistance, including *S. pseudintermedius* (e.g., MRSP), are disk diffusion  $\leq 17$  mm and MIC  $\geq 0.5$  mcg/mL. If staphylococci are resistant to oxacillin, they should be interpreted as being resistant to all cephalosporins and penicillins, regardless of sensitivity result. Oxacillin resistance is usually interpreted as equivalent to methicillin resistance; therefore oxacillin-resistant staphylococci are also referred to as MRSA or MRSP.

## Formulations

- Oxacillin is available in 250- and 500-mg capsules and 50-mg/mL oral solution.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Oxacillin is soluble in water and alcohol. The reconstituted oral solution is stable for 3 days at room temperature and 14 days in the refrigerator.

## Small Animal Dosage

### Dogs and Cats

- 22-40 mg/kg q8h PO.

## Large Animal Dosage

- No doses are reported. Oral absorption has not been established for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. Oral absorption has not been established for ruminants. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Oxazepam

oks-ay'zeh-pam

**Trade and other names:** Serax

**Functional classification:** Anticonvulsant

## Pharmacology and Mechanism of Action

Benzodiazepine. Oxazepam is a central-acting CNS depressant with action similar to diazepam. Its mechanism of action appears to be via potentiation of gamma aminobutyric acid (GABA)-receptor-mediated effects in the CNS. Oxazepam is one of the active products of metabolism from diazepam. In contrast to diazepam, oxazepam does not undergo extensive hepatic metabolism in animals, but it is glucuronidated before excretion. In dogs, oxazepam has a half-life of 5-6 hours, but these values were derived from administration of the parent drug diazepam. Oxazepam is eliminated by direct conjugation with glucuronide, without other intermediate metabolites produced, whereas diazepam and other benzodiazepines may produce other intermediate active metabolites.

## Indications and Clinical Uses

Oxazepam is used for sedation and to stimulate appetite. The appetite-stimulating effects have been used, particularly in cats that may have diminished appetites caused by other primary diseases. It has been more potent than diazepam as an appetite stimulant in cats. As a benzodiazepine, it also may be considered for behavior problems and anxiety disorders in animals, but it has not been used as commonly as other drugs.

### Precautionary Information

#### Adverse Reactions and Side Effects

Sedation is the most common side effect. It may also produce polyphagia. Some animals may experience paradoxical excitement. Chronic administration may lead to dependence and a withdrawal syndrome if discontinued.

#### Contraindications and Precautions

Oral administration of another benzodiazepine—diazepam—has caused severe idiosyncratic liver injury in cats. It is not known if the same concern applies to oxazepam, which is a metabolite of diazepam, although no cases of liver injury from oxazepam have been reported.

#### Drug Interactions

Use cautiously with other drugs that may cause sedation.

## Instructions for Use

Doses based on empiricism. There have been no clinical trials in veterinary medicine, although it is widely believed to increase the appetite in cats.

## Patient Monitoring and Laboratory Tests

Samples of plasma or serum may be analyzed for concentrations of benzodiazepines. Plasma concentrations in the range of 100-250 ng/mL have been cited as the therapeutic range for people. Other references have cited this range as 150-300 ng/mL. However, there are no readily available tests for monitoring in many veterinary laboratories. Laboratories that analyze human samples may have nonspecific tests for benzodiazepines. With these assays, there may be cross-reactivity among benzodiazepine metabolites.

## Formulations

- Oxazepam is available in 10-, 15-, and 30-mg capsules and 15- and 30-mg tablets.

## Stability and Storage

Stable if stored in manufacturer's original formulation. Although oxazepam has been compounded for veterinary use, the potency and stability have not been evaluated for compounded products.

## Small Animal Dosage

### Cats

- Behavior disorders: 0.2-0.5 mg/kg q12-24h PO or 1-2 mg/cat q12h PO.
- Appetite stimulant: 2.5 mg/cat PO. The maximum effect is from 1 mg/kg, but doses as low as 0.1 mg/kg have been effective.

### Dogs

- Behavior disorders or sedation: 0.2-1 mg/kg q12-24h PO. For some indications it has been administered q6h.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

Schedule IV controlled drug

RCI Classification: 2

## Oxfendazole

oks-fen'dah-zole

**Trade and other names:** Benzelmin and Synanthic

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Antiparasitic drug. Oxfendazole belongs to the benzimidazole class of antiparasitic drugs. Like other benzimidazole drugs, it produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in parasites, eventually resulting in death. However, there is no effect on glucose metabolism in mammals. It is used to treat intestinal parasites in animals.

## Indications and Clinical Uses

Oxfendazole is used in horses for treatment of large roundworms (*Parascaris equorum*), mature and immature pinworms (*Oxyuris equi*), large strongyles (*Strongylus edentatus*, *Strongylus vulgaris*, and *Strongylus equinus*), and small strongyles. In cattle, fendazole is used for treatment of lungworms (*Dictyocaulus viviparus*), stomach worms (barberpole worms [*Haemonchus contortus* and *H. placei*, adult]), small stomach worms (*Trichostrongylus axei*, adult), brown stomach worms (*Ostertagia ostertagi*), intestinal worms, nodular worms (*Oesophagostomum radiatum*, adult), hookworms (*Bunostomum phlebotomum*, adult), small intestinal worms (*Cooperia punctata*, *C. oncophora*, and *C. momasteri*), and tapeworms (*Moniezia benedeni*, adult).

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse reactions are rare.

### Contraindications and Precautions

Do not administer to sick or debilitated horses. Do not administer to female dairy cattle of breeding age.

### Drug Interactions

No drug interactions are reported.

## Instructions for Use

Administer to horses by mixing in a suspension and administering orally (e.g., via stomach tube) or mixing pellets with food. Administer to cattle orally with a dose syringe or intraruminally with a rumen injector. Treatment may be repeated in 6-8 weeks in horses or in 4-6 weeks in cattle.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Oxfendazole is available in a 90.6- or 225-mg/mL suspension (cattle), 185-mg/gram paste (cattle), 0.375 g per gram of paste (equine), 90.6-mg/mL suspension (equine), and 6.49% pellets (equine).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. After mixing for oral administration, discard unused portion after 24 hours. Mix well before using, do not freeze suspension, and avoid excessive heat.

## Small Animal Dosage

### Dogs and Cats

- Dose has not been established.

## Large Animal Dosage

### Horses

- 10 mg/kg PO.

### Cattle

- 4.5 mg/kg PO.

## Regulatory Information

Do not use in dairy cattle.

Cattle slaughter withdrawal time: 7 days for suspension; 11 days for paste.

## Oxibendazole

oks-ih-ben'dah-zole

**Trade and other names:** Anthelcide EQ

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Antiparasitic drug. Oxibendazole belongs to the benzimidazole class of antiparasitic drugs. Like other benzimidazole drugs, it produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in parasites, eventually resulting in death.



However, there is no effect on glucose metabolism in mammals. It is used to treat intestinal parasites in animals.

## Indications and Clinical Uses

Oxibendazole is used in horses for treatment of large strongyles (*Strongylus edentatus*, *S. equinus*, and *S. vulgaris*), small strongyles (species of the genera *Cylicostephanus*, *Cylicocyclus*, *Cyathostomum*, *Triodontophorus*, *Cylicodontophorus*, and *Gyalocephalus*), large roundworms (*Parascaris equorum*), pinworms (*Oxyuris equi*) including various larval stages, and threadworms (*Strongyloides westeri*).

Formulations for dogs may contain both diethylcarbamazine citrate and oxibendazole for prevention of *Dirofilaria immitis* (heartworm disease) and *Ancylostoma caninum* (hookworm infection) and for treatment of *Trichuris vulpis* (whipworm infection) and intestinal *Toxocara canis* (Ascarid infection).

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse reactions are rare. Occasional vomiting and nausea may occur in dogs.

### Contraindications and Precautions

Do not administer to dogs that may have heartworms.

### Drug Interactions

No drug interactions are reported.

## Instructions for Use

Administer suspension to horses by mixing with 1-2 L of water (3-4 pints) and administering orally (e.g., via stomach tube). Alternatively, mix powder with grain ration or use the paste. Horses should be retreated in 6-8 weeks if they are reexposed. For dogs, medication may be mixed with food daily.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Oxibendazole is available in 10% suspension; 22.7% paste; and 60-, 120-, and 180-mg diethylcarbamazine citrate + 45-, 91-, and 136-mg oxibendazole tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Mix well before using, do not freeze suspension, and avoid excessive heat.

## Small Animal Dosage

### Dogs

- 5 mg/kg oxibendazole (combined with 6.6 mg/kg diethylcarbamazine) q24h PO.

### Cats

- No dose established.

## Large Animal Dosage

### Horses

- 10 mg/kg PO.
- Threadworms: 15 mg/kg PO once. Retreat in 6-8 weeks if necessary.

## Regulatory Information

No withdrawal times are established.

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Oxtriphylline

oks-trih'fih-lin

**Trade and other names:** Choledyl-SA

**Functional classification:** Bronchodilator

### Pharmacology and Mechanism of Action

Choline theophyllinate. Methylxanthine bronchodilator. Free theophylline is released after absorption. Mechanism of action is unknown, but may be related to increased cyclic adenosine monophosphate (cAMP) levels or antagonism of adenosine. There appears to be anti-inflammatory and bronchodilating action.

### Indications and Clinical Uses

Oxtriphylline is used for similar respiratory conditions, as is theophylline. It is indicated in patients with reversible bronchoconstriction, such as dogs with airway disease. The use of oxtriphylline has diminished considerably, and it is more convenient and preferable to administer theophylline in most cases. Large animal uses have not been reported.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects include nausea, vomiting, and diarrhea. With high doses, tachycardia, excitement, tremors, and seizures are possible. Cardiovascular and CNS adverse effects appear to be less frequent in dogs than in people.

#### Contraindications and Precautions

Some patients may be at a higher risk for adverse effects. Such patients may include animals with cardiac disease, animals prone to arrhythmias, and animals at risk for seizures.

#### Drug Interactions

Drugs that inhibit cytochrome P450 enzymes may increase drug concentrations and cause toxicity. See Appendix I for a list of drugs that may be P450 inhibitors.

### Instructions for Use

Some formulations (Theocron) contain oxtriphylline and guaifenesin. When administering a slow-release tablet, do not crush it. Theophylline, which may be more readily available, may be substituted for oxtriphylline.

### Patient Monitoring and Laboratory Tests

Therapeutic drug monitoring is recommended for chronic therapy. Interpretation of theophylline concentrations should be used to guide therapy. Generally, 10-20 mcg/mL is considered therapeutic.

### Formulations

- Oxtriphylline is available in 400- and 600-mg tablets. (Oral solutions and syrup are available in Canada but not in the US.)

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 47 mg/kg (equivalent to 30 mg/kg theophylline) q12h PO.

## Large Animal Dosage

- No doses have been reported for large animals. Oral absorption has not been established for ruminants.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Oxybutynin Chloride

oks-ih-byoo'tih-nin klor'ide

**Trade and other names:** Ditropan

**Functional classification:** Anticholinergic

## Pharmacology and Mechanism of Action

Anticholinergic agent. Oxybutynin produces an anticholinergic effect via blockade of muscarinic receptors. It will produce a general anticholinergic effect, but the predominant effect is on the urinary bladder. It inhibits smooth muscle spasms via blocking action of acetylcholine. It does not block skeletal muscle, autonomic ganglia, or receptors on blood vessels. A related drug used in people is tolterodine (Detrol).

## Indications and Clinical Uses

Oxybutynin chloride has been used primarily to increase bladder capacity and to decrease spasms of the urinary tract. In people, it is used to treat urinary incontinence, but the use in animals is not common.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are related to anticholinergic effects (atropinelike effects), but they are less frequent compared to other anticholinergic drugs. Constipation, dry mouth, and dry mucous membranes are possible from routine use. If an overdose occurs, administer physostigmine for treatment.

### Contraindications and Precautions

Use cautiously in animals with heart disease or decreased intestinal motility. Use cautiously in animals with glaucoma.

### Drug Interactions

Oxybutynin will potentiate other antimuscarinic drugs.

## Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Although it increases urine retention, it may not be effective to treat incontinence in animals with decreased sphincter tone.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Oxybutynin is available in 5-mg tablets and 1-mg/mL oral syrup.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Oxybutynin is soluble in water and ethanol.

## Small Animal Dosage

### Dogs

- 0.2 mg/kg q12h PO; for larger dogs, use 5 mg/dog q6-8h PO.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. Oral absorption has not been established for ruminants. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Oxymetholone

oks-ih-meth'oh-lone

**Trade and other names:** Anadrol

**Functional classification:** Hormone, anabolic agent

## Pharmacology and Mechanism of Action

Anabolic steroid. Oxymetholone is a derivative of testosterone. Anabolic agents are designed to maximize anabolic effects while minimizing androgenic action. Anabolic agents have been used for reversing catabolic conditions, increasing weight gain, increasing muscling in animals, and stimulating erythropoiesis. Other anabolic agents include boldenone, nandrolone, stanozolol, and methyltestosterone.

## Indications and Clinical Uses

Anabolic agents have been used for reversing catabolic conditions, increasing weight gain, increasing muscling in animals, and stimulating erythropoiesis. Although other anabolic agents have been used in animals (methyltestosterone and stanozolol), there are no differences in efficacy among the anabolic steroids demonstrated in animals.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects from anabolic steroids can be attributed to the pharmacologic action of these steroids. Increased masculine effects are common. Increased incidence of some tumors has been reported in people. The 17 $\alpha$ -methylated oral anabolic steroids (oxymetholone, stanozolol, and oxandrolone) have been associated with hepatic toxicity.

### Contraindications and Precautions

Do not use in pregnant animals.

### Drug Interactions

No drug interactions are reported.

## Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

## Patient Monitoring and Laboratory Tests

Monitor hepatic enzymes for evidence of cholestasis and hepatotoxicity.

## Formulations

- Oxymetholone is available in 50-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats**

- 1-5 mg/kg/day PO.

**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

Oxymetholone is a Schedule III controlled drug.

Do not administer to animals intended for food.

RCI Classification: 4

**Oxymorphone Hydrochloride**

oks-ih-mor'fone hye-droe-klor'idē

**Trade and other names:** Numorphan

**Functional classification:** Analgesic, opioid

**Pharmacology and Mechanism of Action**

Opioid agonist and analgesic. Action is similar to morphine, except that oxymorphone is 10-15 times more potent than morphine. Action is to bind to mu-opiate and kappa-opiate receptors on nerves and inhibit release of neurotransmitters involved with transmission of pain stimuli (such as substance P). Central sedative and euphoric effects related to mu-receptor effects in the brain. Other opiates used in animals include hydromorphone, codeine, morphine, meperidine, and fentanyl. In dogs, the half-life is 0.8 hours (IV) and 1 hour (SQ), with high clearance rates ( $>50$  mL/kg/min). In cats, the half-life is 1.7 hours, with clearance of 26 mL/kg/min. Effective concentrations are not established for animals, but in people they range from 2.5-4.5 ng/mL.

**Indications and Clinical Uses**

Oxymorphone is indicated for short-term analgesia, for sedation, and as an adjunct to anesthesia. It is compatible with most anesthetics and can be used as part of a multimodal approach to analgesia/anesthesia. Although oxymorphone is FDA-approved for dogs, other opiates are used more commonly such as hydromorphone and morphine. Administration of oxymorphone may lower dose requirements for other anesthetics and analgesics used. Duration of action in dogs is short (2-4 hours). The oral dose formulations are only 10% absorbed in people but should not be relied on for treating severe pain in dogs.

**Precautionary Information****Adverse Reactions and Side Effects**

Like all opiates, side effects from oxymorphone are predictable and unavoidable. Side effects from opiate administration include sedation, vomiting, constipation, urinary retention, and bradycardia. Panting may occur in dogs as a result of changes in thermoregulation. Histamine release, known to occur from administration of morphine, may be less likely with oxymorphone. Excitement can occur in some animals, but it is more common in cats and horses. Respiratory depression occurs with high doses. As with other opiates, a slight decrease in heart rate is expected. In most cases, this decrease does not have to be treated with anticholinergic drugs (e.g., atropine), but it should be monitored. Tolerance and dependence occur with chronic administration. In horses,

undesirable and even dangerous behavior actions can follow rapid IV opioid administration. Horses should receive a preanesthetic of acepromazine or an  $\alpha_2$  agonist.

### Contraindications and Precautions

Oxymorphone is a Schedule II controlled substance. Cats and horses may be more sensitive to opiates.

### Drug Interactions

Like other opiates, it will potentiate other drugs that cause CNS depression.

## Instructions for Use

There is some evidence that oxymorphone may have fewer cardiovascular effects compared to morphine. Oxymorphone is more readily absorbed systemically from epidural administration compared to morphine. Oxymorphone may be used with acepromazine and other sedatives; together they have synergistic effects.

## Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

## Formulations

- Oxymorphone is available in 1.5- and 1-mg/mL injection. Five- and 10-mg tablets are available but have not been shown to be absorbed in animals.

## Stability and Storage

The pH of solution is 2.7-4.5. Oxymorphone is compatible with most fluid solutions. Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- Analgesia: 0.1-0.2 mg/kg IV, SQ, or IM (as needed); redose with 0.05-0.1 mg/kg q1-2h. A dose of 0.25 mg/kg SQ q6h may be used for less severe pain.
- Preanesthetic: 0.025-0.05 mg/kg IM or SQ.
- Sedation: 0.05-0.2 mg/kg (with or without acepromazine) IM or SQ.
- Cats: 0.03 mg/kg bolus IV, followed by 0.02 mg/kg every 2 hours; or constant-rate infusion (CRI) with a loading dose of 5 mcg/kg, followed by 5 mcg/kg/hr infusion.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Schedule II controlled drug.

RCI Classification: 1

## Oxytetracycline

oks'ih-tet-rah-sye'kleen

**Trade and other names:** Terramycin, Terramycin Soluble Powder, Terramycin Scours Tablets, Bio-Mycin, Oxy-Tet, and Oxybiotic Oxy 500 and Oxy 1000. Long-acting formulations include Liqueamycin-LA 200 and Bio-Mycin 200.

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Tetracycline antibiotic. Mechanism of action of tetracyclines is to bind to 30S ribosomal subunit and inhibit protein synthesis. Oxytetracycline is usually bacteriostatic. It has a broad spectrum of activity, including gram-positive and gram-negative bacteria, some protozoa, *Rickettsiae*, and *Ehrlichiae*. The spectrum also includes *Chlamydia*, spirochetes, *Mycoplasma*, L-form bacteria, and some protozoa (*Plasmodium* and *Entameba*). Resistance is common among gram-negative bacteria of the *Enterobacteriaceae* (e.g., *Escherichia coli*). Oxytetracycline has been available in a variety of formulations to control the release rate from an injection. Vehicles include polyethylene glycol, propylene glycol, povidone, or pyrrolidine. Although oral preparations are available, oral absorption is poor. For example, oral absorption of 44 mg/kg in dogs was variable and too low to produce therapeutic effects. In pigs, oral absorption was only 4% (compared to chlortetracycline, which is 13%). Most pharmacokinetic studies have been performed with injectable oxytetracycline. After IM injection in cattle, the half-life is approximately 21 hours, with a maximum concentration ( $C_{MAX}$ ) of 5.6 mcg/mL. In horses, the half-life (IV) was approximately 10-13 hours. In pigs, the half-life (IV) was approximately 4-6 hours.

## Indications and Clinical Uses

Oxytetracycline is used to treat infections of the respiratory tract (pneumonia), urinary tract, soft tissues, and skin. It is used for infections caused by a wide spectrum of bacteria, except that resistance is common among gram-negative bacilli of enteric origin and staphylococci. One of the most common uses is in cattle for treatment of bovine respiratory disease (BRD) caused by *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni* (formerly *Haemophilus somnus*). In pigs, tetracyclines have been used to treat atrophic rhinitis, pneumonic pasteurellosis, and *Mycoplasma* infections. In small animals, doxycycline, rather than oxytetracycline, is used as a treatment for *Rickettsiae* and *Ehrlichiae*. In horses, oxytetracycline has been administered to treat equine piroplasmosis caused by *Theileria equi*, but was not effective for *Babesia caballi*. Oxytetracycline has been used for treating Potomac fever in horses caused by *Neorickettsia risticii*, as well as respiratory and soft tissue infections. In newborn horses, oxytetracycline has been administered at high doses for the purpose of correcting angular limb deformities. The doses have been as high as 50-70 mg/kg IV q48h. This effect may be caused by a decrease in the viscoelastic properties in the tendons of young animals. Because this produces tendon or ligament laxity, it may correct angular limb deformities in young foals.

## Precautionary Information

### Adverse Reactions and Side Effects

Tetracyclines may cause renal tubular necrosis at high doses, but this is rare with recommended doses. Tetracyclines can affect bone and teeth formation in young animals. (Note that in studies cited above for treatment of young foals, no adverse effects were observed.) They have been implicated in drug fever in cats. Hepatotoxicity may occur at high doses in susceptible individuals. Oxytetracycline administration to horses has been associated with colic and diarrhea.

### Contraindications and Precautions

Use cautiously in young animals because teeth discoloration is possible. Avoid injection volumes for IM greater than 10 mL per site in cattle and greater than 5 mL in pigs.

### Drug Interactions

Tetracyclines bind to compounds containing calcium, which decreases oral absorption. Do not mix with solutions that contain iron, calcium, aluminum, or magnesium.

## Instructions for Use

Oral dose forms are for large animal use. Use of injectable long-acting forms has not been studied in small animals. Use of tetracyclines in small animals has primarily relied on doxycycline or minocycline. For large animals, there is both a conventional and long-acting formulation. The long-acting formulation contains a viscosity excipient used to prolong the absorption from the injection site. One such excipient is 2-pyrrolidone. When using long-acting formulations, the long-acting properties only apply to IM use, not IV administration. When products that are long acting are compared to conventional injectable products, the long-acting products usually allow for longer dose intervals. However, in pigs, there were no differences in duration of plasma concentrations when equivalent doses were administered.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive cattle respiratory pathogens is  $\leq 2$  mcg/mL, and  $\leq 0.5$  mcg/mL for swine respiratory pathogens. For other organisms, the break point is  $\leq 2$  mcg/mL for streptococci and  $\leq 4$  for other organisms. Tetracycline can be used as a marker to test susceptibility for other drugs in this class, such as doxycycline and minocycline.

## Formulations

- Oxytetracycline is available in 250-mg tablets; 500-mg bolus; 100- and 200-mg/mL injection; and 25-, 166-, and 450-g/lb of powder. Long-acting formulations are available in a 200-mg/mL injection. Oxytetracycline hydrochloride soluble powder is available to be added to drinking water for poultry, cattle, and pigs. Oxytetracycline is available as a medicated feed for cattle, poultry, fish, and pigs.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. If solutions are diluted prior to injection, they should be discarded if not used immediately. Solution may darken slightly without losing potency.

## Small Animal Dosage

### Dogs and Cats

- 7.5-10 mg/kg q12h IV or 20 mg/kg q12h PO.

## Large Animal Dosage

### Horses

- Treatment of ehrlichiosis (Potomac fever caused by *N. risticii*) and other infections: 10 mg/kg q24h IM or IV (slowly). (IM injections can cause pain and reactions at injection site.)
- Treatment of equine piroplasmiasis: 5-6 mg/kg once daily IV for 7 days.

### Foals

- Treatment of flexural limb deformities: 44 mg/kg, up to 70 mg/kg (2-3 g per foal), two doses 24 hours apart.

### Calves

- 11 mg/kg/day PO.
- Treatment of pneumonia: 11 mg/kg q12h PO.

### Cattle

- Injection for treatment of anaplasmosis, enteritis, pneumonia, and other infections: 11 mg/kg q12h IV.
- Long-acting formulations: 20 mg/kg IM as a single dose.



**Pigs**

- 6.6-11 mg/kg, up to 10-20 mg/kg, q24h IM or 20 mg/kg q48h IM.

**Regulatory Information**

Cattle and pig withdrawal times for meat: 7 days (oral tablets). For oral soluble powder, the withdrawal times vary greatly from one product to another for cattle and pigs. Generally, they are at least 5 days for meat, but consult specific product label for withdrawal times.

Cattle withdrawal times for injection: 18-22 days, depending on the product.

Cattle withdrawal times for long-acting formulations: 28 days.

Cattle withdrawal times for milk: 96 hours at a dose of 20 mg/kg.

Cattle withdrawal times (intrauterine administration): 7 days for milk and 28 days for meat. Cattle withdrawal times (intramammary administration): 6 days for milk and 28 days for meat.

Pig withdrawal times: 28 days and up to 42 days, depending on product.

**Oxytocin**

oks-ih-toe'sin

**Trade and other names:** Pitocin, Syntocinon (nasal solution), and generic brands

**Functional classification:** Labor induction

**Pharmacology and Mechanism of Action**

Oxytocin stimulates uterine muscle contraction via action on specific oxytocin receptors. When administered around the time of luteolysis, it stimulates prostaglandin F receptor (PGF<sub>2</sub>)-alpha secretion and disrupts luteolysis. When administered prior to luteolysis, it does not induce PGF<sub>2</sub>-alpha and disrupts luteolysis and prolongs corpus luteum function.

**Indications and Clinical Uses**

Oxytocin is used to induce or maintain normal labor and delivery in pregnant animals. In surgery, it may be used postoperatively following cesarean section to facilitate involution and resistance to the large inflow of blood. In large animals, oxytocin is used to augment uterine contractions and stimulate lactation. It will contract smooth muscle cells of the mammary gland for milk letdown if the udder is in a proper physiological state. It is also used to expel the placenta after delivery. However, efficacy for retained placenta is questionable, and some experts believe that estrogen should be administered in addition to oxytocin. Oxytocin does not increase milk production, but it will stimulate contraction leading to milk ejection. Oxytocin administered prior to luteolysis (prior to day 10 postovulation in horses) prolongs corpus luteum function and suppresses estrus behavior in mares.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are uncommon if used carefully. However, careful monitoring of labor is necessary during its use.

**Contraindications and Precautions**

Do not administer to pregnant animals unless for induction of parturition. Do not administer unless cervix is fully relaxed. Do not use if there is abnormal presentation of the fetus.

**Drug Interactions**

Beta-adrenergic agonists will inhibit induction of labor.

### Instructions for Use

Oxytocin is used to induce labor. In people, oxytocin is administered via injection, constant IV infusion, or intranasal solution.

### Patient Monitoring and Laboratory Tests

Fetal stress and progression of normal labor should be monitored closely.

### Formulations

- Oxytocin is available in 10- and 20-units/mL injection and 40-units/mL nasal solution.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 5-20 units per dog IM or SQ (repeat every 30 min for primary inertia). Note: Manufacturer's label lists higher doses of 5-30 units per dog.

#### Cats

- 2.5-3 units per cat IM or IV. Repeat up to three times every 30-60 minutes. (Maximum dose is 3 units/cat).

### Large Animal Dosage

- **Note:** The following doses are all on a per-animal basis rather than a per-kilogram basis and some doses from experts may vary from the approved label dose.

#### Cattle

- To stimulate uterine contractions: 30 units IM and repeat in 30 minutes if necessary. (Manufacturer lists 100 units per cow.)
- For retained placenta: 20 units IM given immediately after calving and repeated in 2-4 hours.
- For milk letdown: 10-20 units per cow IV or IM.

#### Mares

- To stimulate uterine contractions: 20 units IM. (Manufacturer lists 100 units per mare.)
- For retained placenta: 30-40 units IM at 60- to 90-minute intervals or add 80-100 units to 500 mL saline solution and give IV.
- To suppress estrus behavior in mares: 60 units per mare IM once or twice daily on days 7-14 postovulation.

#### Small Ruminants and Sows

- 5-10 units IM. (Manufacturer lists 30-50 units per animal.)

### Regulatory Information

No withdrawal times have been reported. Because of low risk of residues and rapid clearance after administration, a 24-hour withdrawal time is suggested.

## Paclitaxel

Pak'li tax'el

**Trade and other names:** Paccal Vet-CA1 (veterinary formulation), Abraxane and Taxol (human formulations)

**Functional classification:** Anticancer agent, Antineoplastic

### Pharmacology and Mechanism of Action

Paclitaxel is an anticancer agent used in dogs for some neoplasms. It is a natural product derived from the western yew tree and obtained via a semisynthetic process from *Taxus baccata*. Paclitaxel is in the class of drugs called *taxanes*, which are tubulin-protein active drugs for treating cancer.

From paclitaxel, there is also the semisynthetic drug docetaxel. These drugs differ from vincristine and vinblastine. They bind to a different site on the tubulin protein and promote, rather than inhibit, mitotic spindle formation. The mitotic spindles formed are aberrant and disrupt the mitotic phase of the cell cycle. These drugs promote the assembly of microtubules from tubulin dimers and stabilize microtubules by preventing depolymerization. This stability results in the inhibition of the normal dynamic reorganization of the microtubule network that is essential for vital interphase and mitotic cellular functions. These drugs may be active in other parts of the cell cycle, as they induce abnormal microtubules throughout the cell cycle and multiple asters of microtubules during mitosis.

In dogs, pharmacokinetic studies demonstrate that the terminal half-life may be as long as 12 hours in some dogs, with high volume of distribution.

### Indications and Clinical Uses

Paclitaxel and the related drug docetaxel are used for a variety of cancers in people (e.g., breast cancer) as part of a chemotherapy regimen. In dogs, paclitaxel has been used for mammary carcinoma and squamous cell carcinoma, and perhaps other tumors. Paclitaxel also has been used in dogs for mast cell tumors (MCTs).

### Precautionary Information

#### Adverse Reactions and Side Effects

The human formulation, which contains Cremophor EL (polyoxyethylated castor oil) as a carrier vehicle, can cause severe anaphylactoid reactions in dogs and should be avoided. Adverse effects in dogs from the veterinary form are primarily related to bone marrow suppression. The most severe neutropenia usually occurs in 5-7 days after administration. Thrombocytopenia, vomiting, and constipation also are possible. As with many other anticancer agents, vomiting, diarrhea, and nausea are common.

Do not use in dogs that are pregnant, lactating, or intended for breeding. Paclitaxel is a teratogen and can affect female and male fertility. Laboratory studies in the rat have shown reduced fertility, embryotoxicity, teratogenicity, and maternal toxicity.

#### Contraindications and Precautions

Because this is an anticancer agent, standard precautions should be applied when using this agent in animals. These precautions include following manufacturer's recommendations for safe handling of the vials and syringes, and disposing of infusion supplies.

Do not use in dogs that are pregnant, lactating, or intended for breeding. Paclitaxel is a teratogen and can affect female and male fertility.

### Drug Interactions

No known drug interactions have been reported in dogs. However, paclitaxel is metabolized by cytochrome P450 isoenzymes and is a P-glycoprotein (P-gp) substrate. Therefore interactions are possible when administered with other drugs that may inhibit these systems, or in dogs that have a deficiency in P-gp. Because most anticancer agents are often administered with other agents, complications from multiple drugs are possible.

## Instructions for Use

The manufacturer has provided detailed instructions for safe administration. The powder of the veterinary formulation requires reconstitution before use. After reconstitution with lactated Ringer's solution, the solution contains 1 mg of paclitaxel/mL. Gently swirl the vial by hand for 20 to 30 seconds. Protect from light and allow the vial to stand for 3 to 5 minutes. Gently and slowly swirl and/or invert the vial until the powder is completely dissolved. Do not shake—this will result in foaming. If foam develops, allow the solution to stand for several minutes. Reconstitution can continue even if all of the foam has not dissipated. If undissolved product is present, the vial should be placed on a shaker and rotated for up to 15 minutes while protected from light. The solution should be clear and greenish-yellow without visible precipitates. If precipitates or discoloration (orange-reddish) are observed, the solution should be discarded. After the solution is determined to be appropriate for injection, administer the appropriate amount into an empty, sterile ethyl vinyl acetate (EVA) infusion bag. Protect the reconstituted product in the EVA infusion bag from light. The reconstituted product should be used immediately. The appropriate dose should be infused intravenously over 15-30 minutes. Compatibility with other infusion sets is undetermined.

## Patient Monitoring and Laboratory Tests

The most severe adverse effect is bone marrow suppression. Monitor complete blood count (CBC) to determine if doses need adjustment to prevent severe neutropenia. If dogs develop severe neutropenia ( $< 2000$  cells/ $\mu$ L) or have a concurrent serious infection, withhold treatment.

Paclitaxel can cause gastrointestinal adverse reactions due to transient gastrointestinal mucosal cell toxicity. Monitor patients carefully for vomiting, diarrhea, and dehydration. Provide supportive care as clinically indicated.

## Formulations

- The human formulation is formulated in Cremophor EL (polyoxyethylated castor oil). This vehicle is associated with significant anaphylactoid reactions in dogs and should be avoided. Instead, the veterinary formulation is preferred, which does not contain this carrier (Paccal Vet-CA1). The veterinary formulation is in a 60-mg vial to be reconstituted to 1 mg/mL. Paclitaxel is highly lipophilic and practically insoluble in water. The veterinary formulation is composed of micellar nanoparticles, which is suitable for aqueous administration.

## Stability and Storage

Store the unopened vials in the refrigerator and protect from light. After opening and reconstitution, use the reconstituted product immediately because it does not contain a preservative. After reconstitution according to manufacturer's instructions,

the solution contains 1 mg of paclitaxel/mL. It should be protected from light throughout the preparation process. According to the manufacturer, the powder should be greenish-yellow to yellow. In case of discoloration, discard the vial. Let the vials stand protected from light at room temperature for approximately 20 to 30 minutes. The room temperature should not exceed 25° C (77° F).

### Small Animal Dosage

#### Dogs

- 150 mg/m<sup>2</sup> IV over 15-30 minutes, once every three weeks for up to four doses. (Dose range has been 130-150 mg/m<sup>2</sup>.) If adverse reactions develop, reduce dose by increments of 10 mg/m<sup>2</sup> or delay the time for administration.

#### Cats

- No doses have been established for cats at this time, but there are anecdotal accounts of its safe use in cats.

### Large Animal Dosage

- No doses have been reported for large animals.

### Regulatory Information

Because this is an anticancer agent, it is forbidden to administer to food-producing animals.

## Pamidronate Disodium

pam-ih-droe'nae dye-soe'dee-um

**Trade and other names:** Aredia

**Functional classification:** Antihypercalcemic

### Pharmacology and Mechanism of Action

Bisphosphonate drug. Drugs in this class include pamidronate, etidronate, tiludronate, and pyrophosphate. These drugs are characterized by a germinal bisphosphonate bond, which slows the formation and dissolution of hydroxyapatite crystals. The drugs' clinical use resides in their ability to inhibit bone resorption. They decrease bone turnover by inhibiting osteoclast activity, inducing osteoclast apoptosis, retarding bone resorption, and decreasing the rate of osteoporosis. Inhibition of bone resorption is via inhibition of the mevalonate pathway. Pamidronate, like other bisphosphonates, is not metabolized by the liver. It is primarily eliminated by the kidneys in animals, and preferentially remains in the bone for prolonged periods.

### Indications and Clinical Uses

Pamidronate, like other bisphosphonate drugs, is used in people to treat osteoporosis and treatment of hypercalcemia of malignancy. In animals, pamidronate is used to decrease calcium in conditions that cause hypercalcemia, such as cancer and vitamin D toxicosis. It is helpful for managing neoplastic complications and pain associated with pathologic bone resorption. It also may provide pain relief in patients with pathologic bone disease and may reduce glucocorticoid-induced osteoporosis. Experimental work performed in dogs has shown it to be effective for treating cholecalciferol toxicosis, but it did not prevent decreases in renal function. After treating for hypercalcemia in dogs, the duration of effect was 11 days to 9 weeks (median

8.5 weeks). Some bisphosphonates (see tiludronate, and clodronate) are approved to treat bone pain in horses caused by navicular disease.

### Precautionary Information

#### Adverse Reactions and Side Effects

Fever, joint pain, and myalgias have been observed, but otherwise no serious adverse effects have been identified. However, the use in animals has not been common enough to identify a wider range of adverse effects. One study in dogs reported a slight decrease in food intake. In humans, acute renal necrosis after IV administration has been reported. Because pamidronate is eliminated by the kidneys in dogs, a dose-dependent nephropathy is possible and the risk of renal injury is more likely with doses exceeding 3 mg/kg IV. In people, there is some concern that the use of bisphosphonates produces excessive mineralization and hardening of the bone, which may result in a greater risk of fractures. However, this effect has not been reported for animals.

#### Contraindications and Precautions

Although SQ administration is listed in dose protocols, the IV route is preferred. Do not administer to animals with kidney disease, and ensure animals are well hydrated prior to administration. Do not administer to animals with conditions that may be associated with hypocalcemia.

#### Drug Interactions

Do not mix with solutions containing calcium (e.g., lactated Ringer's solution).

### Instructions for Use

For IV infusion, dilute in fluid solution (0.9% saline) and administer over 2 hours. (Dilute 30 mg pamidronate in 250 mL fluids.) Infusion can be repeated every 7 days. Although the SQ route is listed for some veterinary applications, it is not recommended and IV infusion is the preferred route.

### Patient Monitoring and Laboratory Tests

Monitor serum calcium and phosphorus. Treatment of vitamin D toxicosis with pamidronate may result in decreased renal function. Monitor urea nitrogen, creatinine, urine-specific gravity, and food intake in treated animals.

### Formulations

- Pamidronate is available in 30-, 60-, and 90-mg vials for injection and 1 mg/mL in single-use vials for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Vials may be diluted in fluid solutions (e.g., 250 mL 0.9% sodium chloride) and infused over 2 hours or as long as 24 hours. Diluted solutions are stable for 24 hours at room temperature.

### Small Animal Dosage

#### Dogs

- Treatment for hypercalcemia: 1-2 mg/kg IV or SQ.
- Treating malignant osteolytic disease: 1-2 mg/kg IV every 28 days as a 2-hour IV infusion.
- Treatment of cholecalciferol toxicosis: 1.3-2 mg/kg IV or SQ for two treatments after toxin exposure.

**Cats**

- Treatment of hypercalcemia: 1-1.5 mg/kg, IV.

**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

**Pancrelipase**

pan-kreh-lye'pase

**Trade and other names:** Viokase, Pancrezyme, Cotazym, Creon, Pancoate, Pancrease, and Ultrase

**Functional classification:** Pancreatic enzyme

**Pharmacology and Mechanism of Action**

Pancreatic enzyme. Pancrelipase provides lipase, amylase, and protease. Pancrelipase is a mixture of enzymes (lipase, amylase, and protease) obtained from the pancreas of pigs. These enzymes enhance digestion of fats, proteins, and starches in the upper duodenum and jejunum. They are more active in an alkaline environment. There are coated and uncoated tablets. The uncoated tablets are not as bioavailable because degradation may occur in the acid of the stomach. Each milligram contains 24 units lipase, 100 units amylase, and 100 units of protease activity.

**Indications and Clinical Uses**

Pancrelipase is used to treat pancreatic exocrine insufficiency. It provides enzymes lacking for digestion. It should be administered before meals. It is inactivated in gastric acid and should be administered with a drug to suppress stomach acid (e.g., H<sub>2</sub>-receptor blocker or proton pump inhibitor [PPI]) to improve activity.

**Precautionary Information****Adverse Reactions and Side Effects**

Oral bleeding has been reported from administration of tablets. The tablets contain potent enzymes, and contact with mucosal membranes may cause lesions and mucosal ulcers. Ensure that tablets are not trapped in the esophagus, or esophageal erosions may occur. Warn owners that if they handle tablets, avoid hand-to-mucosa contact (e.g., contact with eyes).

**Contraindications and Precautions**

Enteric-coated tablets may not be as effective as mixing powder with food.

**Drug Interactions**

If antacids are used concurrently, magnesium hydroxide and calcium carbonate may reduce effectiveness.

**Instructions for Use**

Mix pancrelipase with food when administering approximately 20 minutes prior to feeding. After successful results are obtained, the dose may be reduced gradually to

identify the minimum effective dose. Pancreatic enzymes are more effective if administered with acid-suppressing drugs ( $H_2$  blockers, PPIs, bicarbonate, or some antacids). If delayed-release capsules are used (granules), do not crush. Different brands have varying activity. If switching from one brand to another, not all products will result in the same therapeutic results.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Pancrelipase is available in a composition of 16,800 units of lipase, 70,000 units of protease, and 70,000 units of amylase per 0.7 g. It is also available in capsules and tablets. Various formulations contain a variety of activity. For example, Viokase powder contains 16,000 units/70,000 units/70,000 units (lipase/protease/amylase) per 0.7 g of powder. Tablets range from 8000/30,000/30,000 units (lipase/protease/amylase) to 11,000/30,000/30,000 units (lipase/protease/amylase) per tablet. The delayed-release capsules (Creon) are available as 6000 units/19,000 units/30,000 units; or 12,000 units/38,000 units/60,000 units; or 24,000 units/76,000 units/120,000 units (lipase/protease/amylase) per tablet.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It is inactivated in an acid environment.

### Small Animal Dosage

#### Dogs

- Mix 2 teaspoon (tsp) of powder with food per 20 kg body weight or 1-3 tsp/0.45 kg of food 20 minutes prior to feeding. Formulations with granules in capsules may be opened and sprinkled on food (approximately 1 capsule with meals for a dog).

#### Cats

- Mix one half teaspoon per cat with food.

### Large Animal Dosage

- No doses have been reported for large animals.

### Regulatory Information

Because of low risk of residues and rapid clearance after administration, no withdrawal time is suggested.

## Pancuronium Bromide

pan-kyoo-roe'nee-um bro'mide

**Trade and other names:** Pavulon

**Functional classification:** Muscle relaxant

### Pharmacology and Mechanism of Action

Neuromuscular blocking agent (nondepolarizing). Pancuronium, like other drugs in this class, competes with acetylcholine at the neuromuscular end plate to produce paralysis. Sensory nerves are intact.



## Indications and Clinical Uses

Pancuronium is a paralytic agent used during anesthesia or for mechanical ventilation. It is used primarily during anesthesia or other conditions in which it is necessary to inhibit muscle contractions. It is sometimes used as an alternative to atracurium because it is longer acting.

### Precautionary Information

#### Adverse Reactions and Side Effects

Pancuronium produces respiratory depression and paralysis. Neuromuscular blocking drugs have no effect on analgesia.

#### Contraindications and Precautions

Do not use in patients unless mechanical ventilation support can be provided.

#### Drug Interactions

Some drugs may potentiate the action (e.g., aminoglycosides) and should not be used concurrently.

## Instructions for Use

Administer only in situations in which careful control of respiration is possible. Doses may need to be individualized for optimum effect. Do not mix with alkalinizing solutions or lactated Ringer's solution.

## Patient Monitoring and Laboratory Tests

Monitor patient's respiration rate, heart rate, and rhythm during use. If possible, monitor the oxygenation status during anesthesia.

## Formulations

- Pancuronium is available in a 1- and 2-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- 0.1 mg/kg IV, or start with 0.01 mg/kg and additional 0.01-mg/kg doses q30min.
- Constant-rate infusion (CRI): 0.1 mg/kg IV, followed by 2-mcg/kg/min infusion.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). Racing Commissioners International (RCI) Classification: 2

## Pantoprazole

pan-toe-pray'zole

**Trade and other names:** Protonix

**Functional classification:** Antiulcer agent

## Pharmacology and Mechanism of Action

Proton pump inhibitor. Pantoprazole inhibits gastric acid secretion by inhibiting the  $K^+/H^+$  pump. Pantoprazole, like other PPIs, has potent and long-acting effects. Acid suppression may have a duration >24 hours in animals. Other PPIs that are administered orally (e.g., omeprazole) have been used in animals. Pantoprazole is the first PPI that can be administered IV. After a dose, it inhibits acid secretion for >24 hours.

## Indications and Clinical Uses

Pantoprazole is used for treatment and prevention of gastrointestinal ulcers. Other PPIs include omeprazole, lansoprazole (Prevacid), and rabeprazole (AcipHex). All PPIs act via a similar mechanism and are equally effective. However, there has been more experience with omeprazole in animals than the other drugs of this group. In dogs, pantoprazole (1 mg/kg) maintained stomach pH >3-4 when administered IV. Pantoprazole, being the only one in an IV formulation, is often used when an IV drug is preferred for treatment.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects have not been reported in animals. However, in people there is concern about hypergastrinemia with chronic use. Overgrowth of *Clostridium* bacteria has been a concern from chronic use because of chronic gastric acid suppression, but the clinical importance of this concern in animals has not been established.

### Contraindications and Precautions

No known contraindications.

### Drug Interactions

Do not mix IV solution with other drugs. Do not administer with drugs that depend on stomach acid for absorption (e.g., ketoconazole, itraconazole, iron supplements). Proton pump inhibitors may inhibit some drug-metabolizing enzymes (CYP450 enzymes), although in people there was low risk of drug interactions caused by enzyme inhibition. In people there may be an increased risk of intestinal injury when proton pump inhibitors are administered with NSAIDs, but this has not been studied in animals.

## Instructions for Use

For treating gastrointestinal ulcers, administer once per day for 7-10 days. For gastrin-secreting tumors, use higher dose (1 mg/kg) twice daily. Other PPIs include omeprazole (Prilosec), lansoprazole (Prevacid), and rabeprazole (AcipHex). They all act via a similar mechanism and are equally effective. The primary difference with pantoprazole is that it is available in an IV dosage formulation and can be mixed with fluid solutions. For IV use, mix a 40-mg vial with 10 mL saline and further dilute with saline, lactated Ringer's solution, or 5% dextrose to 0.4 mg/mL. Administer IV infusion over at least 15 minutes.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. When treating ulcers, monitor hematocrit or CBC to detect bleeding. Monitor for signs of vomiting and diarrhea.

## Formulations

- Pantoprazole is available in a 40-mg vial for IV use (diluted to 4 mg/mL) and 20- and 40-mg delayed-release tablets. There are also granules for oral suspension (40 mg), which have been mixed with apple juice or applesauce for administration in people.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze reconstituted solutions. Once diluted for IV use, it is stable for 12 hours.

## Small Animal Dosage

### Dogs and Cats

- 0.5-0.6 mg/kg once daily PO.
- Intravenous administration (24 hours): 0.5-1 mg/kg IV infusion over 24 hours. This dose may be delivered in 2 or 15 minutes (see next).
- Intravenous administration (2 or 15 minutes): First flush IV line. Administer pantoprazole via IV line with dextrose 5% injection, sodium chloride 0.9% injection, or Ringer's lactate injection. For 2-minute infusion, mix 40 mg of powder with 10 mL of sodium chloride 0.9% injection for a final concentration of 4 mg/mL. Infuse 1-mg/kg dose over 2 minutes. For 15-minute infusion, mix 40-mg vial with 10 mL sodium chloride 0.9% injection. Then further admix this solution with 100 mL of dextrose 5% injection, sodium chloride 0.9% injection, or Ringer's lactate injection to a total volume of 110 mL, producing a solution with a final concentration of approximately 0.4 mg/mL. Administer final dose (1 mg/kg) over 15 minutes.

## Large Animal Dosage

- No dose is reported for large animals. Doses have been extrapolated from human use (0.5 mg/kg q24h IV), and infusion protocols listed previously for small animals have been used.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use with withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 5

## Paregoric

pare-eh-gore'ik

**Trade and other names:** Corrective mixture

**Functional classification:** Antidiarrheal

## Pharmacology and Mechanism of Action

Paregoric (opium tincture) is an outdated product used to treat diarrhea. Paregoric contains 2 mg of morphine in every 5 mL of paregoric. The action is via stimulation of intestinal mu-opiate receptors to cause a decrease in intestinal peristalsis.

## Indications and Clinical Uses

Paregoric will decrease signs of diarrhea via opiate effects, but its use is somewhat outdated.

## Precautionary Information

### Adverse Reactions and Side Effects

Like all opiates, side effects are predictable and unavoidable. Side effects may include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses. Tolerance and dependence occur with chronic administration.

### Contraindications and Precautions

Contains opium and may be abused by humans. Use cautiously in horses and ruminants because intestinal motility may be decreased.

### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Use of paregoric has been replaced by more specific products such as loperamide or diphenoxylate.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- For every 5 mL of paregoric, there is 2 mg of morphine.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 0.05-0.06 mg/kg q12h PO.

### Large Animal Dosage

- No doses have been reported for large animals.

### Regulatory Information

Schedule III Controlled Substance. Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Paromomycin Sulfate

pare-oe-moe-mye'sin sul'fate

**Trade and other names:** Humatin

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Antibiotic drug of the aminoglycoside class. The mechanism of action of paromomycin is similar to other aminoglycosides: It inhibits the ribosomal 30S subunit with subsequent inhibition of bacterial protein synthesis. Spectrum of activity is similar to other aminoglycosides. However, because paromomycin is administered orally and generally not absorbed systemically, its activity is limited to intestinal pathogens.

### Indications and Clinical Uses

The use of paromomycin is limited to intestinal infections. It is not absorbed systemically and should not be used for extraintestinal infections. Paromomycin has been used to treat intestinal infections, such as cryptosporidiosis. The use is based on limited accounts in animals and extrapolation from humans. Efficacy in animals has not been tested in controlled studies.

**Precautionary Information****Adverse Reactions and Side Effects**

Paromomycin has been associated with renal failure and blindness when used in cats. Although systemic absorption is not expected to be high, cats treated with high doses for intestinal organisms developed problems.

**Contraindications and Precautions**

Extreme caution is recommended when administering this drug to animals that may have a compromised bowel resulting from intestinal disease because increased systemic absorption may occur.

**Drug Interactions**

No drug interactions have been reported in animals.

**Instructions for Use**

In cats, doses of 125-165 mg/kg every 12 hours have been administered for 5-7 days PO. However, there are reports in the veterinary literature that these doses have produced toxicity in cats, including kidney injury. It is suggested to use lower doses to avoid toxicity and monitor the patient's renal parameters carefully. When there is a compromised integrity of the intestinal mucosa, as may occur with diarrhea, use of paromomycin is discouraged.

**Patient Monitoring and Laboratory Tests**

Monitor patient's renal function, such as urine-specific gravity, serum creatinine, and blood urea nitrogen (BUN), during treatment.

**Formulations**

Paromomycin is available in 250-mg capsules.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Cats**

- Doses of 125-165 mg/kg q12h PO for 7 days have been recommended. However, caution is recommended when using doses this high. Lower doses should be considered (see [dog dose](#)) in animals that may be at risk of toxicity.

**Dogs**

- The dose in dogs has been extrapolated from human medicine, which is 10 mg/kg q8h PO for 5-10 days.

**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. Although not absorbed systemically to a large extent, it is expected that concentrations may persist in the kidneys, producing long, extended withdrawal times for slaughter.

## Paroxetine

par-oks'eh-teen

**Trade and other names:** Paxil

**Functional classification:** Behavior modification

### Pharmacology and Mechanism of Action

Antidepressant drug. Paroxetine, like other drugs in this class, is classified as a selective serotonin reuptake inhibitor (SSRI). It resembles fluoxetine (Reconcile, Prozac) in action. Its mechanism of action appears to be via selective inhibition of serotonin reuptake and downregulation of 5-HT<sub>1</sub> receptors. Selective serotonin reuptake inhibitor drugs are more selective for inhibiting serotonin reuptake than the tricyclic antidepressant (TCA) drugs.

### Indications and Clinical Uses

Paroxetine, like other SSRI drugs, is used to treat behavioral disorders such as compulsive disorders (canine compulsive disorder), anxiety, and dominance aggression. In cats, it has been effective for decreasing urine spraying. Because of the small tablet size, some veterinarians have found it easy to administer to cats and small dogs.

### Precautionary Information

#### Adverse Reactions and Side Effects

Some effects similar to fluoxetine, but in some animals paroxetine is better tolerated. Adverse effects observed in dogs and cats include constipation and decreased appetite. Decreased appetite in cats is more common at higher doses.

#### Contraindications and Precautions

Use cautiously in patients with heart disease. Do not use in pregnant animals. There is a risk of fetal malformations if used early in pregnancy.

#### Drug Interactions

Do not use with monoamine oxidase inhibitors (MAOIs), such as selegiline. Do not use with other behavior-modifying drugs, such as other SSRIs or TCAs.

### Instructions for Use

Dosing recommendations are empirical. Paroxetine has been used for conditions similar to what has been treated with fluoxetine (Prozac, Reconcile). In cats, the small tablet size has made it easier to administer convenient doses, compared to chewable tablets or other drugs available in capsules. Paroxetine has caused constipation in some animals, and veterinarians may administer a feline laxative for the first week of therapy to avoid problems.

### Patient Monitoring and Laboratory Tests

Use in animals has been relatively safe, and one should only monitor behavior changes.

### Formulations

- Paroxetine is available in 10-, 20-, 30-, and 40-mg tablets and 2-mg/mL oral suspension.

### Stability and Storage

Stable if stored in manufacturer's original formulation. Although paroxetine has been compounded for veterinary use, the potency and stability have not been evaluated for compounded products.

## Small Animal Dosage

### Dogs

- 0.5 mg/kg/day PO. For some compulsive disorders, increase the dose to 1 mg/kg q24h PO.

### Cats

- One eighth to one fourth of a 10-mg tablet per cat daily PO (approximately 0.5 mg/kg q24h). For urine spraying in cats, some have responded to every-other-day treatment.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

RCI Classification: 2

## Penicillamine

pen-ih-sill'ah-meen

**Trade and other names:** Cuprimine and Depen

**Functional classification:** Antidote

## Pharmacology and Mechanism of Action

Penicillamine is also called 3-mercaptopalane. It is a chelating agent for lead, copper, iron, and mercury. When used to treat copper toxicity, it helps to solubilize copper in the cells to allow for more rapid urinary excretion. Treated animals should have increased copper urinary excretion. Other drugs that have been used as chelating agents include tetrathiomolybdate, trientine, and zinc. Penicillamine also has anti-inflammatory properties. It inhibits collagen cross-linking by making it more susceptible to enzyme degradation. This antifibrotic property may contribute to its positive effect for treating animals with hepatitis; however, efficacy for this indication has been questioned (see below).

## Indications and Clinical Uses

Penicillamine has been used in people to treat rheumatoid arthritis. The primary use in animals is primarily for treatment of copper toxicity and hepatitis associated with accumulation of copper. Treatment duration for animals with copper-storage hepatic disease may require 2-4 months. It also has been used to treat cystine calculi. Although it may inhibit collagen and reduce fibrosis in patients with hepatic disease, this effect has been disappointing in clinical patients. There is no clear demonstration that it is efficacious for this indication.

Penicillamine has recently become expensive for use in animals, and other alternatives are being investigated. An alternative to consider, if formulations are available, is trientine (triethylenetetramine dihydrochloride), another copper chelating agent. Trientine has been administered to dogs at a dose of 10-15 mg/kg q12h PO.

## Precautionary Information

### Adverse Reactions and Side Effects

The most common adverse effects are anorexia and vomiting. In people, allergic reactions, cutaneous reactions, agranulocytosis, and anemia have been reported. It has also produced proteinuria and hematuria, and in cats has caused neutropenia. In dogs treated for liver disease, corticosteroid-like hepatopathy has been observed. Therefore it may produce steroid-like effects in the liver.

### Contraindications and Precautions

Do not use in pregnant animals. There appears to be little cross-reaction between penicillin and penicillamine in allergic animals.

### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

Administer on an empty stomach (at least 30-60 minutes before meals).

## Patient Monitoring and Laboratory Tests

Monitor liver biochemistry tests during treatment. Monitor metal concentrations if used to treat intoxication.

## Formulations

Penicillamine is available in 125- and 250-mg capsules and 250-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Penicillamine is soluble in water. Preparations of penicillamine in a suspension for oral use have been combined with syrups and flavorings and were stable for 5 weeks.

## Small Animal Dosage

### Dogs and Cats

- 10-15 mg/kg q12h PO, best administered 30 minutes before a meal.
- Doberman pinschers: use 250 mg per dog q12h PO.

## Large Animal Dosage

### Horses and Cattle

- 10-15 mg/kg q12h PO.

## Regulatory Information

Cattle withdrawal time: 21 days for meat; 3 days for milk.

## Penicillin G

**Trade and other names:** Penicillin G potassium or sodium, Penicillin G benzathine (Benza-Pen), Penicillin G, Procaine, and generic Penicillin V (Pen-Vee)

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Penicillin G is also called benzyl penicillin. Its action is similar to other penicillins. It binds penicillin-binding proteins (PBPs) to weaken or cause lysis of the cell wall. Penicillin G is bactericidal with a time-dependent action. An



increased bactericidal effect is observed when drug concentrations are maintained above minimum inhibitory concentration (MIC) values. The spectrum of penicillin G is limited to gram-positive bacteria, anaerobic bacteria, and a few highly susceptible gram-negative bacteria (e.g., *Pasteurella* spp.). Practically all bacteria of the *Enterobacteriaceae* and beta-lactamase-producing *Staphylococcus* spp. are resistant. Penicillin sodium or penicillin potassium when injected intravenously has a half-life of 1 hour or less in most animals. However, the same dose of procaine penicillin given intramuscularly may produce more prolonged concentrations and a half-life of 20-24 hours because of slow absorption from the injection site.

Formulations of penicillin G are designed to control the absorption from site of injection. Formulations include:

- Sodium or potassium penicillin G (crystalline penicillin), which is water soluble and can be administered intravenously or intramuscularly. It may also be mixed with fluids for IV administration.
- Penicillin G benzathine, which is insoluble and available as a suspension. It is slowly absorbed from an injection site to produce low but prolonged (several days of) penicillin concentrations. All benzathine penicillin G forms are combined with procaine penicillin G in commercial formulation (1:1 ratio).
- Penicillin G procaine is a poorly soluble suspension for intramuscular or subcutaneous administration. It is absorbed slowly, producing concentrations for 12-24 hours after injections.
- Penicillin V, oral penicillin, is not highly absorbed and has a narrow spectrum in comparison with other penicillin derivatives.

### Indications and Clinical Uses

Penicillin G is administered by injection either intravenously (potassium or sodium penicillin) or intramuscularly (procaine or procaine/benzathine penicillin G). Penicillin G is indicated for treatment of gram-positive cocci that cause respiratory infections, abscesses, and urinary tract infections (UTIs). Many staphylococci are resistant because of beta-lactamase synthesis. Streptococci are usually susceptible. Other susceptible organisms include gram-positive bacilli and anaerobic bacteria. Most gram-negative bacilli, especially those of enteric origin, are resistant. Some gram-negative respiratory pathogens such as *Pasteurella multocida* and *Mannheimia haemolytica* are susceptible.

Penicillin concentrations in the urine are at least 100-fold higher than plasma concentrations in treated animals; therefore some urinary pathogens may be more susceptible.

### Precautionary Information

#### Adverse Reactions and Side Effects

Penicillin G is usually well tolerated. Allergic reactions are possible. Diarrhea is common with oral doses. Pain and tissue reactions may occur with IM or SQ injections. Formulations of procaine penicillin G contain varying amounts of free procaine (depending on the formulation). Free procaine in the formulation may elicit a central nervous system (CNS) reaction after injection in some horses. Large doses of sodium penicillin IV can decrease potassium concentrations.

#### Contraindications and Precautions

Use cautiously in animals allergic to penicillin-like drugs. Avoid injection volumes greater than 30 mL per site. Administration of the long-acting benzathine form of penicillin G will increase the risk of residues in food-producing animals.

#### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

The approved dose listed on the injectable product labels are outdated and do not reflect the current clinical use of penicillin. Penicillin G benzathine is not recommended for most infections because concentrations are too low to provide therapeutic drug concentrations. A possible exception is for treatment of streptococcal infections. Avoid SQ injection with procaine penicillin G because of tissue injury and food-animal residue problems. Penicillin V should be administered on an empty stomach for maximum absorption.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) break point for susceptible equine pathogens (*Streptococcus equi* and *Staphylococcus* spp.) is  $\leq 0.5$  mcg/mL. The break point for bovine isolates causing bovine respiratory disease is  $\leq 0.25$  mcg/mL. The CLSI break points for susceptible organisms isolated from people are  $\leq 8$  mcg/mL for enterococci and  $\leq 0.12$  mcg/mL for staphylococci and streptococci.

## Formulations

- Penicillin G potassium is available in 5- to 20-million-unit vials. Penicillin G benzathine is available in 150,000 units/mL and is usually combined with 150,000 units/mL of procaine penicillin G suspension. Benzathine penicillin products are not recommended. Procaine penicillin G is available in 300,000-units/mL suspension. Penicillin is one of the few antibiotics that is still measured in terms of units rather than weight in milligrams or micrograms. One unit of penicillin represents the specific activity in 0.6 mcg of sodium penicillin. Thus 1 mg of penicillin sodium represents 1667 units of penicillin. In some references, an approximate conversion of 1000 units per mg is used.
- Penicillin V is available in 250- and 500-mg tablets (250 mg is equal to 400,000 units).

## Stability and Storage

Sodium and potassium forms of penicillin G retain their potency for 72 hours at room temperature, but refrigeration is recommended. It is stable for 7 days if refrigerated and retains 90% potency for 14 days. Penicillin potassium and penicillin sodium are freely soluble in water. One gram of penicillin will dissolve in 250 mL of water (4 mg/mL). Degradation and inactivation of penicillin solutions are accelerated at high pH (pH  $>8$ ), strong acids, or oxidizing agents.

## Small Animal Dosage

- Penicillin G potassium or sodium: 20,000-40,000 units/kg q6-8h IV or IM.
- Procaine penicillin G: 20,000-40,000 units/kg q12-24h IM.
- Penicillin V: 10 mg/kg q8h PO.

## Large Animal Dosage

### Cattle and Sheep

- Procaine penicillin G: 22,000-66,000 units/kg q24h IM. Subcutaneous use is discouraged.
- Sodium or potassium penicillin G: 20,000 units/kg IM or IV q6h.

### Pigs

- Procaine penicillin G: 15,000-25,000 units/kg q24h IM.

**Horses**

- Penicillin sodium or penicillin potassium: 20,000-24,000 units/kg q6-8h IV. (Doses up to 44,000 units/kg q6h have been used for refractory cases.)
- Procaine penicillin G: 20,000-24,000 units/kg q24h IM.
- Potassium penicillin G: 20,000-24,000 units/kg q12h IM.

**Regulatory Information**

Horses: Injections of procaine penicillin may cause a positive test for procaine prior to racing for as long as 30 days after an injection.

Withdrawal times for benzathine penicillin at label dose of 6000-7000 units/kg in cattle: 30 days for meat (14 days in Canada).

Withdrawal times for procaine penicillin at label dose of 6000-7000 units/kg in cattle: 10 days for meat, 4 days for milk; sheep, 9 days; swine, 7 days.

Withdrawal times for procaine penicillin G at a dose of 15,000 units/kg in pigs: 8 days.

Withdrawal times for procaine penicillin G at a dose of 21,000 units/kg in cattle: 10 days for meat, 96 hours for milk.

Procaine penicillin G at a dose of 60,000 units/kg: 21 days for cattle, 15 days for pigs. RCI Classification: Penicillin is not classified; procaine 3

**Pentastarch**

**Trade and other names:** Pentaspan

**Functional classification:** Fluid replacement

**Pharmacology and Mechanism of Action**

Pentastarch is a synthetic colloid volume expander that is used to maintain vascular volume in animals with circulatory shock. It is prepared from hydroxyethyl starch and is derived from amylopectin. There are two hydroxyethyl starch preparations: hetastarch and pentastarch. Hetastarch (6%) has an average molecular weight of 450,000 and colloid osmotic pressure of 32.7. Pentastarch (10%) has an average molecular weight of 280,000 and colloid osmotic pressure of 40. Because hetastarch is a larger molecular weight compound than pentastarch, it tends to remain in the vasculature and prevent loss of intravascular volume and tissue edema. After administration, pentastarch will be retained in the vasculature and prevent loss of intravascular volume and tissue edema. Other colloids used are dextrans (Dextran 40 and Dextran 70). Hetastarch and the dextrans are discussed in other sections.

**Indications and Clinical Uses**

Pentastarch is used primarily to treat acute hypovolemia and shock. It is administered intravenously in acute situations. Pentastarch has a duration of effective volume expansion of 12-48 hours. Pentastarch is used in similar situations as hetastarch, but it is used less frequently.

## Precautionary Information

### Adverse Reactions and Side Effects

There has only been limited use in veterinary medicine; therefore adverse effects have not been reported. However, it may cause allergic reactions and hyperosmotic renal dysfunction. Coagulopathies are possible but are rare and less likely than with hetastarch.

### Contraindications and Precautions

No contraindications are reported for animals.

### Drug Interactions

Pentastarch is compatible with most fluid solutions.

## Instructions for Use

Pentastarch is used in critical care situations and is infused via CRI. Pentastarch may be more effective and produce fewer side effects than Dextran. Because of lower molecular weight, it can be infused more quickly than hetastarch.

## Patient Monitoring and Laboratory Tests

Monitor patient's hydration status and blood pressure during administration.

## Formulations

- Pentastarch is available in a 10% injectable solution.

## Stability and Storage

Pentastarch is stable in original packaging. Compatible with most fluid administration sets.

## Small Animal Dosage

### Dogs

- CRI: 10-25 mL/kg/day IV.

### Cats

- CRI: 5-10 mL/kg/day IV.

## Large Animal Dosage

### Horses

- 8-15 mL/kg or delivered as CRI 0.5-1 mL/kg/hr IV.
- No doses have been reported for other large animals.

## Regulatory Information

No regulatory requirements.

## Pentazocine

pen-taz'oh-seen

**Trade and other names:** Talwin-V

**Functional classification:** Analgesic, opioid

## Pharmacology and Mechanism of Action

Synthetic opiate analgesic. The action of pentazocine results from its effect as a mu-opiate receptor partial agonist and a kappa-receptor agonist. Most of the sedative and analgesic effects are believed to be caused by the kappa-receptor effects. Pentazocine

## 618 Pentazocine

may partially reverse some mu-receptor agonist effects. Its effects are believed to be similar to buprenorphine or butorphanol, but efficacy is less.

### Indications and Clinical Uses

Pentazocine has been used for sedation and analgesia, primarily in horses. However, because of the availability of other opioids with better efficacy, the use of pentazocine has declined.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are similar to other opioid analgesic drugs and include constipation, ileus, vomiting, and bradycardia. Sedation is common at analgesic doses. Respiratory depression can occur with high doses. Dysphoric effects are possible in some sensitive individuals and in some species (e.g., horses).

#### Contraindications and Precautions

Pentazocine is a Schedule IV controlled substance.

#### Drug Interactions

Pentazocine may potentiate other sedative drugs such as alpha<sub>2</sub>-agonists. Pentazocine may interfere with mu-opiate effects of other drugs, such as morphine or fentanyl.

### Instructions for Use

Pentazocine is a mixed agonist/antagonist. It is relatively modest to weak in efficacy for pain control, and other opioids should be considered for better pain management.

### Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

### Formulations

Pentazocine is available in a 30-mg/mL injection (availability has been limited).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 1.65-3.3 mg/kg q4h IM or as needed.

#### Cats

- 2.2-3.3 mg/kg q4h IM, IV, or SQ or as needed.

### Large Animal Dosage

#### Horses

- 200-400 mg per horse IV.

### Regulatory Information

Pentazocine is a Schedule IV controlled drug. Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873 -2723).

RCI Classification: 3

## Pentobarbital Sodium

pen-toe-bar'bih-tahl soe'dee-um

**Trade and other names:** Nembutal and generic brands

**Functional classification:** Anesthetic, barbiturate

### Pharmacology and Mechanism of Action

Short-acting barbiturate anesthetic. The action of pentobarbital is via nonselective depression of CNS. Duration of action may be 3-4 hours.

### Indications and Clinical Uses

Pentobarbital is usually used as an IV anesthetic. It also is used to control severe seizures in animals for treatment during status epilepticus. In some instances, pentobarbital is included in mixtures used to induce euthanasia in animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are related to anesthetic action. Cardiac depression and respiratory depression are common.

#### Contraindications and Precautions

Rapid IV doses can be lethal. Monitor respiration rate carefully after injection because respiratory depression may occur.

#### Drug Interactions

Pentobarbital will potentiate sedative and cardiorespiratory-depressing effects of other anesthetics. Pentobarbital is subject to effects from other drugs that may either induce or inhibit cytochrome P450 metabolizing enzymes (see Appendix H and I).

### Instructions for Use

Pentobarbital has a narrow therapeutic index. When administering intravenously, inject the first half of the dose initially, then the remainder of the calculated dose gradually until anesthetic effect is achieved.

Most euthanasia solutions contain pentobarbital as their active ingredient. Often other ingredients to facilitate euthanasia are included such as muscle relaxants and drugs with lethal cardiac effects (e.g., edetate disodium 0.05%). The concentration of pentobarbital in most euthanasia solutions is 390 mg/mL with a lethal dose of 1 mL per 10 pounds, which is equivalent to 1 mL per 4.5 kg or 87 mg/kg IV.

### Patient Monitoring and Laboratory Tests

Monitor vital signs, especially heart rate and rhythm and respiration, during anesthesia.

### Formulations

- Pentobarbital has been available in a 50- and 65-mg/mL solution for injection (contains propylene glycol). The availability has been inconsistent from some suppliers but it is currently available from veterinary distributors. Some manufacturers discontinued production because of objection to its use for lethal injection during executions.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. pH of solution is 9-10.5 and may affect stability of other coadministered drugs. It will precipitate if combined with most hydrochloride-based drugs or drugs with low

pH. If pentobarbital is used to euthanize animals, it will remain stable even under rendering conditions used for disposal of the carcass.

## Small Animal Dosage

### Dogs and Cats

- General anesthesia: 25-30 mg/kg IV to effect.
- CRI: 2-15 mg/kg IV to effect, followed by 0.2-1 mg/kg/hr.
- Status epilepticus: 2-6 mg/kg IV (15-20 minutes may be needed to take full effect).
- Euthanasia: See “[Instructions for Use](#)” section.

## Large Animal Dosage

### Cattle

- Standing sedation: 1-2 mg/kg IV.

### Cattle, Sheep, and Goats

- General anesthesia: 20-30 mg/kg IV given to effect.

## Regulatory Information

If used for a euthanasia agent, the carcass should not be fed to other animals or used for food. Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule II controlled drug

RCI Classification: 2

## Pentoxifylline

pen-toks'ih-fill-in

**Trade and other names:** Trental, oxpentifylline, and generic brands

**Functional classification:** Anti-inflammatory agent

## Pharmacology and Mechanism of Action

Methylxanthine. Pentoxifylline is used primarily as a rheological agent in people (increases blood flow through narrow vessels). An improved rheological effect has also been demonstrated with equine red blood cells but not neutrophils. As a phosphodiesterase inhibitor (PDE 4 inhibitor), it also produces anti-inflammatory effects. It may have anti-inflammatory action via inhibition of cytokine synthesis. Pentoxifylline suppresses synthesis of inflammatory cytokines, such as interleukin-1 (IL-1 beta), IL-2, IL-6, and tumor necrosis factor (TNF) alpha and may inhibit lymphocyte activation. In experimental dogs at 20 mg/kg q8h for 30 days, it failed to suppress the acute hypersensitivity reaction, but produced significant inhibition of the late-phase hypersensitivity response.

In horses, the half-life is only 23 minutes and oral absorption has been 45% but variable and inconsistent. Pentoxifylline undergoes extensive hepatic metabolism in dogs, and systemic availability after oral administration is 50% but can be highly variable and inconsistent. In other studies the oral absorption is only 20%-30% with a short elimination half-life (less than 1 hour). Seven metabolites are produced in animals, with some being biologically active.

## Indications and Clinical Uses

Most of pentoxifylline's use in animals (including doses) is based on anecdotal experience. Pentoxifylline is used in dogs for some dermatoses, vasculitis, contact allergy,

atopy, familial canine dermatomyositis, increased survival of skin flaps, increased healing of radiation injury, and erythema multiforme. In horses, pentoxifylline is used for a variety of conditions in which suppression of inflammatory cytokines or increased blood perfusion is desired. Such conditions have included intestinal ischemia, colic, sepsis, laminitis, and navicular disease. However, the efficacy for treating these diseases has not been shown. It may have improved efficacy for sepsis if combined with a nonsteroidal anti-inflammatory drug (NSAID) (e.g., flunixin).

### Precautionary Information

#### Adverse Reactions and Side Effects

Pentoxifylline may cause effects similar to other methylxanthines, such as nausea, vomiting, and diarrhea. Nausea, vomiting, dizziness, and headache have been reported in people. Vomiting is reported in dogs. Broken tablets taste unpleasant when administered to cats. If crushed tablets are used, plasma concentration will increase more rapidly than with intact tablets, leading to headaches, nausea, and possible vomiting. In horses, IV doses have caused muscle fasciculations, increased heart rate, and sweating.

#### Contraindications and Precautions

None reported. Broken tablets taste unpleasant when administered to cats.

#### Drug Interactions

No drug interactions are reported. However, as a methylxanthine, adverse reactions are possible from coadministration with a cytochrome P450 inhibitor (see Appendix I).

### Instructions for Use

Although pharmacokinetic studies in dogs and horses have been reported, results of clinical studies in animals have been limited. Based on pharmacokinetic studies that show a short half-life in dogs, higher doses than those listed in the dosing section have been advocated. For example, the most effective dose may be as high as 30 mg/kg q8-12h in dogs. Indications for dermatology have used a regimen of every 12 hours, but a frequency of every 8 hours may be considered to get an optimum response in some patients.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Pentoxifylline is available in 400-mg tablets. IV solution is 50 mg/mL.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Aqueous solubility is only 77 mg/mL. Oral suspensions may be stable for up to 90 days, but they will settle, requiring resuspension (shaking) before oral administration.

### Small Animal Dosage

#### Dogs

- Dermatologic use: 10 mg/kg q12h PO, up to 15 mg/kg q8h PO.
- Familial canine dermatomyositis: 25 mg/kg q12h PO.
- Other uses: 10-15 mg/kg q8 PO or 400 mg/dog for most animals.

#### Cats

- One fourth of a 400-mg tablet per cat (100 mg) q8-12h PO.



## Large Animal Dosage

### Horses

- 8.5 mg/kg q8h IV or 10 mg/kg q8h PO (oral absorption is unpredictable).
- Respiratory disease (airway obstruction): 36 mg/kg q12h PO.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 4

## Pergolide, Pergolide Mesylate

per'goe-lide

**Trade and other names:** Prascend (equine formulation), Permax

**Functional classification:** Dopamine agonist

## Pharmacology and Mechanism of Action

Pergolide is used to treat pituitary pars intermedia dysfunction (PPID) in horses, sometimes referred to as “equine Cushing syndrome.” Pergolide is a dopaminergic agonist that stimulates postsynaptic dopamine receptors ( $D_1$  and  $D_2$  receptors). It is a synthetic ergot derivative. In horses with PPID, pergolide stimulates dopamine receptors, resulting in decreased release of adrenocorticotrophic hormone (ACTH), melanocyte-stimulating hormone (MSH), and other proopiomelanocortin peptides. It is capable of stimulating dopamine receptors in conditions in which dopamine is deficient, regardless of the state of the presynaptic dopamine stores. Other drugs that may share similar effects are selegiline, apomorphine, and lisuride (previously called lysuride). In horses, the half-life is 5.9 hours and is rapidly absorbed from oral administration.

## Indications and Clinical Uses

In people, pergolide has been used for neurodegenerative disease in which dopamine is deficient, such as Parkinson disease, in which pergolide is used with levodopa or carbidopa. However, pergolide has been commercially unavailable for humans, and human use diminished because of reports of cardiac valve damage associated with pergolide. In animals, it also has been used for dopamine-deficient states. It is believed that horses and some dogs develop hyperadrenocorticism (Cushing disease)—pituitary-dependent hyperadrenocorticism (PDH)—because of a loss of dopamine antagonism of ACTH release. In horses, it is used successfully to treat PPID (equine Cushing syndrome) and has controlled the disease in horses for longer than 2 years. Most horses with PPID have hyperplasia or adenoma of the pars intermedia of the pituitary. This adenoma is deficient in dopamine and produces excess ACTH. Administration of dopamine agonists acts to suppress ACTH release from the pituitary and subsequently restore cortisol levels to normal states. The benefits of pergolide administration have not been established for dogs or other animals. Because of adverse effects produced, pergolide is not used for treating PDH in dogs.

The pharmacokinetics have been variable, with the manufacturer listing the half-life of 5.9 hours. But other reports listed the half-life as 27 hours. In an IV study in horses, the half-life was 5.6 hours, the mean apparent oral clearance ( $CL/F$ ) was 1204 mL/kg/hr, and the mean apparent volume of distribution ( $V/F$ ) was  $3082 \pm 1354$  mL/kg.

## Precautionary Information

### Adverse Reactions and Side Effects

Pergolide is approved for use in horses and has been evaluated for safety. In field trials, decreased appetite occurred, but was usually transient. Weight loss, lethargy, and behavioral changes have been observed in some horses. Because some horses may have decreased appetite with pergolide, one can start treatment with a lower dose (one half the dose) for the first 2 days in these horses before starting the full dose. Pergolide was withdrawn from the human market because of evidence that drugs that activate the 2b-serotonin receptor (5-HT<sub>2b</sub>) are associated with a distinct form of fibrotic valvulopathy. These effects have not been observed in animals. Pergolide inhibits secretion of prolactin and will increase growth hormone. It may inhibit lactation. Central nervous system effects may include ataxia and dyskinesia. In horses, adverse effects include anorexia, diarrhea, and colic. Worsening of laminitis from pergolide (it is theoretically a vasoconstrictive drug) has not been proved. In dogs, at doses of 100 mcg/kg, it produced significant reactions that included vomiting, tremors, anorexia, restlessness, and diarrhea.

### Contraindications and Precautions

Unlike bromocriptine, pergolide can be used in pregnant animals, but pregnant women or lactating women should avoid exposure. If tablets are broken or crushed, pergolide tablets may cause eye irritation, an irritating smell, or headache. Avoid human exposure and skin contact when preparing tablets for horses.

### Drug Interactions

Pergolide may interact with droperidol and phenothiazines (e.g., acepromazine), and it will exacerbate the effects of selegiline. Do not administer with monoamine oxidase inhibitors (MOAI).

## Instructions for Use

Use in horses is often accomplished by starting with the low dose listed for 4-6 weeks and gradually increase the dose until desired results are obtained. Adjust dose based on clinical response and dexamethasone suppression test or ACTH measurement. It may be possible to obtain better efficacy when pergolide is used concurrently with cyproheptadine, but ordinarily it is used alone. When treating horses, consider supplementing their diet with magnesium and chromium.

## Patient Monitoring and Laboratory Tests

Clinical response to monitor in horses is water consumption, hair shedding, and evidence of laminitis. Adjust doses in horses by monitoring ACTH levels in animals to document pituitary function. In horses, endogenous ACTH concentrations that exceed 27-50 pcg/mL are considered abnormal. Dexamethasone suppression tests can also be performed to monitor treatment in horses. Consult the dexamethasone monograph in this book for the procedure to perform this test. If signs of excessive dosing are observed, decrease the dose by half for 3 to 5 days and then slowly increase in 2-mcg/kg increments every 2 weeks until the desired effect is observed.

## Formulations

- Pergolide is available for horses in 1-mg tablets. Compounded formulations should not be used, as it was shown that these degrade after 14 days. Degradation is accelerated by light and warm temperatures. A color change in the formulation is an indication that degradation has occurred.

### Stability and Storage

Store in a tightly sealed container, protected from light. The stability of compounded formulations is limited, and use of compounded formulations is discouraged.

### Small Animal Dosage

- Small animal doses have not been established but have been extrapolated from human use, which is to start with 1 mcg/kg (0.001 mg/kg) daily PO and increase the dose gradually by 2 mcg/kg at a time until desired effects are observed.

### Large Animal Dosage

#### Horses

- Starting dose: 0.002 mg/kg (2 mcg/kg) q24h PO (1 mg/day for 500-kg horse). After the starting dose, the dosage may be adjusted as needed (e.g., by 1-mcg/kg increments) to effect, up to 4 mcg/kg daily, although a dose of 10 mcg/kg per day has been used in some horses.

### Regulatory Information

Do not administer to animals intended for food.

## Phenobarbital, Phenobarbital Sodium

fee-noe-bar'bih-tahl

**Trade and other names:** Luminal, Phenobarbitone, and generic brands

**Functional classification:** Anticonvulsant

### Pharmacology and Mechanism of Action

Long-acting barbiturate. Phenobarbital has actions similar to other barbiturates on the CNS. However, phenobarbital will produce anticonvulsant effects without significant other barbiturate effects. As an anticonvulsant, it stabilizes neurons by increased chloride conductance via gamma aminobutyric acid (GABA)-mediated channels. The pharmacokinetics have been studied in several animal species. Oral absorption is high in most animals. The half-life after administration ranges from 37-75 hours in dogs, but was longer in some studies. In horses, the half-life is approximately 20 hours, and in cats, the half-life ranges from 35 to 56 hours. In all species, the half-life may be shorter after multiple administration because of autoinduction of hepatic metabolism.

### Indications and Clinical Uses

Phenobarbital is widely used as a drug of choice for treating seizure disorders, such as idiopathic epilepsy, in dogs, cats, horses, and exotic animals. Phenobarbital has been used in foals for treating seizures associated with perinatal encephalopathy. Phenobarbital also has been used as a sedative. Phenobarbital has been effective for the treatment of sialadenosis in dogs caused by submandibular salivary gland enlargement.

### Precautionary Information

#### Adverse Reactions and Side Effects

Most adverse effects are dose related. Phenobarbital causes polyphagia, sedation, ataxia, and lethargy. Some tolerance develops to side effects after initial therapy. Liver enzyme elevations, particularly alkaline phosphatase, are common but may not always be associated with liver pathology. However, hepatotoxicity also has been reported in some dogs and is more likely with high doses. Neutropenia,

anemia, and thrombocytopenia have been associated with phenobarbital therapy in dogs. These reactions are likely to be idiosyncratic and recovery may occur if phenobarbital is discontinued. Combinations of phenobarbital and potassium bromide have increased the risk of pancreatitis in dogs. In dogs, superficial necrolytic dermatitis has been associated with phenobarbital administration without concurrent liver pathology. Affected dogs may have high serum concentrations of phenobarbital.

### Contraindications and Precautions

Administer with caution to animals with liver disease. Phenobarbital may induce its own metabolism, which shortens the half-life. Therefore chronic administration may lower plasma concentrations, resulting in increases in the dose requirement. Pregnant animals may have an increase in seizure frequency, and an increase in dose may be necessary.

### Drug Interactions

Phenobarbital is one of the most potent drugs for inducing hepatic microsomal metabolizing enzymes. Therefore many drugs administered concurrently will have lower (and perhaps subtherapeutic) concentrations because of more rapid clearance. Drugs affected may include theophylline, digoxin, corticosteroids, anesthetics, and other drugs that may be substrates for the P-450 enzymes. Phenobarbital will shorten the half-life of levetiracetam (Keppra) in dogs, which may require higher doses or more frequent administration of levetiracetam. Administration of phenobarbital may lower total T<sub>4</sub> thyroid concentrations, but thyroid-stimulating hormone (TSH) and T<sub>3</sub> concentrations are unaffected. Solutions are alkaline (pH 9-11); therefore avoid mixing with acidic solutions or drugs that will become unstable at alkaline pH.

## Instructions for Use

Adjust dose based on blood levels of phenobarbital. If bromide is used concurrently (sodium or potassium bromide), lower doses of phenobarbital may be used.

Transdermal administration has been examined in cats. Therapeutic concentrations have been achieved if high doses are administered (9 mg/kg q12h) of the PLO gel or Lipoderm transdermal formulation. However, monitoring is suggested because phenobarbital serum concentrations in these cats can be highly variable.

## Patient Monitoring and Laboratory Tests

Phenobarbital doses should be carefully adjusted via monitoring serum/plasma concentrations. Collect a sample at any time during the dose interval because the timing of the sample is not critical. Avoid the use of plasma separation devices if the tube is to be stored (these devices will cause a false lowering of concentrations). The therapeutic range in dogs is considered 15-40 mcg/mL (65-180 mmol/L). If dogs are also receiving bromide, phenobarbital concentrations in the range of 10-36 mcg/mL have been considered therapeutic.

To convert from mmol/L to mcg/mL, use a multiplication factor of 0.232. To convert from mcg/mL to mmol/L, multiply by 4.3.

In cats, the optimum range for therapeutic effect has been reported as 23-28 mcg/mL (99-120 mmol/L) or 15-45 mcg/mL, and in another study was 28-31 mcg/mL. In horses, the optimum range for therapeutic effect is 15-20 mcg/mL (65-86 mmol/L).

Monitor liver enzymes periodically in animals receiving phenobarbital because of risk of hepatopathy. However, some liver enzyme elevations may occur—especially with alkaline phosphatase—without liver pathology. Other liver tests may be needed to rule out hepatotoxicity. Liver enzymes usually return to baseline levels 1-5 weeks after discontinuing treatment. Phenobarbital can increase serum triglycerides because of delayed clearance of chylomicrons from the blood and decreased lipoprotein lipase

(LPL) activity. Monitor CBC periodically in animals treated with phenobarbital because of risk of neutropenia, anemia, and thrombocytopenia. Phenobarbital administration will lower other drug concentrations. Phenobarbital did not interfere with the ACTH stimulation test or low-dose dexamethasone suppression test in dogs. It will lower thyroid  $T_4$  and free  $T_4$  but not  $T_3$  and TSH concentrations in dogs.

### Formulations

- Phenobarbital is available in 15-, 30-, 60-, and 100-mg tablets; 30-, 60-, 65-, and 130-mg/mL injection; and 4-mg/mL oral elixir solution. Because of the bitter taste and alcohol content from the elixir oral liquid formulation, it has been compounded in other vehicles for patients. To prepare this formulation, crush ten 60-mg tablets (600 mg total) and mix with 60 mL Ora Plus and Ora Sweet in a 1:1 ratio for a final concentration of 10 mg/mL. This formulation was stable for 115 days when stored in amber plastic bottles at room temperature. Phenobarbital has been compounded into transdermal formulations for cats, but these have not been evaluated for long-term stability.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Phenobarbital is slightly soluble in water (100 mg/mL), but phenobarbital sodium is more soluble (1 g/mL). Solutions prepared in water have an alkaline pH (9-11). Precipitation may occur at lower pH values (avoid mixing with acidic syrups or flavorings). It is subject to hydrolysis in aqueous solutions. However, if prepared in propylene glycol it is stable for 56 weeks. Stability of compounded formulation is described in the “Formulations” section.

### Small Animal Dosage

#### Dogs

- 2-8 mg/kg q12h PO.
- Status epilepticus: Administer in increments of 10-20 mg/kg IV to effect.

#### Cats

- 2-4 mg/kg q12h PO.
- Status epilepticus: Administer in increments of 10-20 mg/kg IV to effect.

### Large Animal Dosage

#### Horses

- 12 mg/kg q24h PO. Note that in some horses, after initial therapy, higher doses of 12 mg/kg q12h may be needed.
- 5-20 mg/kg IV over 30 minutes (may be diluted in sodium chloride).
- Foals: 2-5 mg/kg IV administered slowly over 20 minutes. Start with lower dose and monitor for effect.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule IV controlled drug

RCI Classification: 2

## Phenoxybenzamine Hydrochloride

fen-oks-ih-ben'zah-meen hye-droe-klor'ide

**Trade and other names:** Dibenzylamine

**Functional classification:** Vasodilator

## Pharmacology and Mechanism of Action

Alpha<sub>1</sub>-adrenergic antagonist. Phenoxybenzamine binds to and antagonizes alpha<sub>1</sub>-receptors on smooth muscle, causing relaxation. It tends to form a permanent covalent bond with adrenergic receptors to produce a long-lasting effect. It is a nonselective alpha-receptor (alpha<sub>1</sub> and alpha<sub>2</sub>) antagonist. It affects both alpha<sub>1a</sub>- and alpha<sub>1b</sub>-receptors. It is a potent and long-acting vasodilator.

## Indications and Clinical Uses

Phenoxybenzamine is used primarily to treat peripheral vasoconstriction. In some animals, it has been used to relax urethral smooth muscle. Urethral smooth muscle is innervated by alpha<sub>1</sub> adrenergic receptors. This property has been used to treat urethral spasm in cats after urethral blockage, although one study in cats found prazosin to be more effective. Experimentally, phenoxybenzamine has been used to relax vascular smooth muscle in horses for treating laminitis. However, this has not been a common clinical use.

## Precautionary Information

### Adverse Reactions and Side Effects

Phenoxybenzamine causes prolonged hypotension in animals. Signs of excessive hypotension may include rapid heart rate, weakness, and syncope. In horses, phenoxybenzamine has caused diarrhea.

### Contraindications and Precautions

Use carefully in animals with cardiovascular compromise. Do not use in dehydrated animals. Use carefully in animals with low cardiac output.

### Drug Interactions

Phenoxybenzamine is a potent alpha-adrenergic antagonist. It will compete with other drugs that act on the alpha-receptor. It will cause vasodilation and should be used cautiously with drugs that may cause vasodilation or depress the heart.

## Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or limited experimental experience in animals.

## Patient Monitoring and Laboratory Tests

Phenoxybenzamine can lower blood pressure significantly. Monitor patient's blood pressure and heart rate if possible during treatment.

## Formulations

Phenoxybenzamine is available in 10-mg capsules. Smaller-sized tablets for cats have been prepared by compounding pharmacies.

## Stability and Storage

Phenoxybenzamine is only slightly soluble in water but soluble in propylene glycol and ethanol. It is not stable in aqueous solutions and undergoes rapid degradation; therefore it may not be stable in some compounded formulations. Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 0.25 mg/kg q8-12h or 0.5 mg/kg q24h PO.
- For presurgical treatment of pheochromocytoma: 0.6 mg/kg q12h (range is 1-2 mg/kg/day), given 2 weeks prior to surgery to stabilize blood pressure.

## 628 Phentolamine Mesylate

### Cats

- 2.5 mg per cat q8-12h or 0.5 mg/kg q12h PO. (Doses as high as 0.5 mg/kg IV have been used to relax urethral smooth muscle.)

### Large Animal Dosage

#### Horses

- 1 mg/kg q24h IV or 0.7 mg/kg q6h PO.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Phentolamine Mesylate

fen-tole'ah-meen mess'ih-late

**Trade and other names:** Regitine and Rogitine (in Canada)

**Functional classification:** Vasodilator

### Pharmacology and Mechanism of Action

Nonselective alpha-adrenergic blocker. Vasodilator. Phentolamine blocks both  $\alpha_1$ - and  $\alpha_2$ -receptors on smooth muscle.

### Indications and Clinical Uses

Phentolamine is a potent vasodilator and is used primarily to treat acute hypertension. It is most useful in hypertensive emergencies.

### Precautionary Information

#### Adverse Reactions and Side Effects

Phentolamine may cause excess hypotension with high doses or in animals that are dehydrated and may cause tachycardia.

#### Contraindications and Precautions

Use carefully in animals with cardiovascular compromise. Do not use in dehydrated animals. Use carefully in animals with low cardiac output.

#### Drug Interactions

Phentolamine is an alpha-adrenergic antagonist. It will compete with other drugs that act on the alpha-receptor. It will cause vasodilation and should be used cautiously with drugs that may cause vasodilation or depress the heart.

### Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. Titrate dose for each patient to produce desired vasodilation.

### Patient Monitoring and Laboratory Tests

Phentolamine can lower blood pressure significantly. Monitor patient's blood pressure and heart rate if possible during treatment.

### Formulations

Phentolamine has been available in 5-mg vials for injection but in the United States may only be available as a bulk powder that must be compounded into a solution.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- 0.02-0.1 mg/kg IV.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Phenylbutazone

fen-ill-byoo'tah-zone

**Trade and other names:** Butazolidin, PBZ, and generic brands

**Functional classification:** Nonsteroidal anti-inflammatory drug

## Pharmacology and Mechanism of Action

Phenylbutazone and other NSAIDs produce analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the cyclooxygenase (COX) enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy gastrointestinal tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects in some situations, and COX-2 activity is important for some biological effects. Phenylbutazone, using in vitro assays, is a nonselective inhibitor of COX-1 and COX-2. It has a half-life of 36-65 days in cattle, 5 hours in horses, and 4-6 hours in dogs.

## Indications and Clinical Uses

Many equine experts believe that phenylbutazone is the most cost-effective treatment for osteoarthritis in horses. The major use of phenylbutazone is in horses for musculoskeletal pain and inflammation, arthritis, soft tissue injury, and racing injuries. It is approved in both dogs and horses. The duration of action in horses after a single administration is approximately 24 hours. Phenylbutazone is approved for use in dogs (and cats in Europe); however, the use in small animals is not common because of the availability of other drugs.

## Precautionary Information

### Adverse Reactions and Side Effects

Although adverse effects have been documented in horses, after 30 years of experience, most equine clinicians have observed good safety with phenylbutazone. Earlier studies that demonstrated common adverse effects may have been exaggerated because the studies were performed in ponies, which is a breed more sensitive than horses. Likewise, draft horses appear to be more sensitive to adverse effects.



Among the adverse effects in horses are gastrointestinal ulcers. Gastric ulcers are more likely as the dose increases and in animals undergoing extensive training. Horses may also develop right dorsal colitis and hypoproteinemia, especially at high doses.

Phenylbutazone has been associated with kidney injury. In horses that are dehydrated or have renal compromise, phenylbutazone can cause ischemia and renal papillary necrosis. In experimental horses, phenylbutazone (4.4 mg/kg q12h for 14 days) decreased proteoglycan synthesis in articular cartilage. However, this effect on articular cartilage with clinical use has not been a documented problem.

Phenylbutazone is rarely used in people because it has caused bone marrow depression, including aplastic anemia. This effect also has been observed in animals.

Phenylbutazone is generally well tolerated in dogs, but there are no data for cats. In these animals, adverse effects possible are gastrointestinal toxicity such as gastritis and gastric ulcers.

### **Contraindications and Precautions**

Do not administer injectable formulation intramuscularly. Do not administer to animals prone to gastrointestinal ulcers or to animals with kidney disease that may become dehydrated. Do not administer with other ulcerogenic drugs, such as corticosteroids.

### **Drug Interactions**

The use with other NSAIDs or with corticosteroids should be done cautiously because of the risk of gastrointestinal injury. Corticosteroids have been shown to exacerbate the gastrointestinal adverse effects. Phenylbutazone has been used in some horses in combination with flunixin meglumine (NSAID “stacking”), but this combination may increase risk of hypoalbuminemia and decreased total serum protein. Phenylbutazone will interfere with the action of furosemide in horses. Some NSAIDs also may interfere with the action of angiotensin-converting enzyme (ACE) inhibitors.

## **Instructions for Use**

Doses are based primarily on manufacturer's recommendations and clinical experience. Although a range of 4.4–8.8 mg/kg per day has been administered to horses, studies have not shown an advantage for the higher dose, and the higher dose of 8.8 mg/kg per day is more likely to cause gastrointestinal injury, hypoalbuminemia, and neutropenia. Generally, a safe starting dose in horses is 4.4 mg/kg every 12 hours IV or PO for 2–3 days. Then the dose should be tapered to 2.2–3.3 mg/kg q12h PO. Combining other NSAIDs with phenylbutazone, such as flunixin (referred to as “stacking”), may improve response when treating lameness and other musculoskeletal problems when compared to phenylbutazone alone. However, this practice must be weighed against an increased risk of gastrointestinal injury.

## **Patient Monitoring and Laboratory Tests**

Monitor CBC for signs of bone marrow toxicity with chronic use.

## **Formulations**

- Phenylbutazone is available in 100-mg, 200-mg, 400-mg and 1-g tablets (bolus); oral paste for horses; and 200-mg/mL (20%) solution for injection.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Phenylbutazone is not water soluble. It should not be compounded in aqueous vehicles.

## Small Animal Dosage

### Dogs

- 15-22 mg/kg q8-12h (44 mg/kg/day; 800 mg/dog maximum) PO or IV.

### Cats

- 6-8 mg/kg q12h IV or PO.

## Large Animal Dosage

### Horses

- 4.4-8.8 mg/kg/day (generally 2 g to 4 g per horse) PO. Typically, a dose of 4.4 mg/kg is administered every 12 hours for the first 2-3 days, followed by a tapering dose to 2.2 mg/kg q12h. It is not recommended to use the highest dose for more than 48-96 hours.
- Injection: 2.2-4.4 mg/kg/day for 48-96 hours. Give injections intravenously only, as IM injections will cause tissue irritation.

### Cattle

- 17-25 mg/kg loading dose, then 2.5-5 mg/kg q24h or 10-14 mg/kg q48h PO or IV. (See regulatory restrictions in cattle.)

### Pigs

- 4 mg/kg q24h IV.

## Regulatory Information

Phenylbutazone is prohibited from use in female dairy cattle younger than 20 months of age. Other withdrawal times have not been established for animals intended for food. However, recommended withdrawal times are 15 days in swine, 40-50 days for slaughter in cattle (oral or IV), and extended to 55 days in cattle if administered intramuscularly.

Residue information for horses: Although it is possible that phenylbutazone residues can occur in horses being slaughtered for food—in jurisdictions where this is allowed—the risk to human health is very low. Some experts do not regard this as a public health issue.

## Phenylephrine Hydrochloride

fen-ill-eſ'rin hye-droe-klor'ide

**Trade and other names:** Neo-Synephrine

**Functional classification:** Vasopressor

## Pharmacology and Mechanism of Action

Alpha<sub>1</sub>-adrenergic receptor agonist. Phenylephrine will stimulate alpha<sub>1</sub>-receptors and cause smooth muscle contraction, primarily in vascular smooth muscle, to cause vasoconstriction. It may be applied topically (e.g., mucous membranes) to constrict superficial blood vessels.

## Indications and Clinical Uses

Phenylephrine is used primarily in critical care patients or during anesthesia to increase peripheral resistance and increase blood pressure. Phenylephrine is also used commonly as topical vasoconstrictor (as in nasal decongestants or for ophthalmic use). It has been administered to horses with nephrosplenic entrapment because the vasoconstriction it produces may produce splenic contraction. Although the incidence of

## 632 Phenylpropanolamine Hydrochloride

severe complications from this treatment in horses is low, phenylephrine-associated hemorrhage is possible with this procedure.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects related to excessive stimulation of  $\alpha_1$ -receptors (prolonged peripheral vasoconstriction). Reflex bradycardia may occur. Prolonged topical use may cause tissue inflammation. When used for treatment of nephrosplenic entrapment in horses, it may cause hemorrhagic shock.

#### Contraindications and Precautions

Do not use in animals with compromised cardiovascular status. It will cause vasoconstriction and can increase blood pressure.

#### Drug Interactions

Phenylephrine will potentiate other  $\alpha_1$ -agonists. Use cautiously with  $\alpha_2$ -agonists such as detomidine, dexmedetomidine, or xylazine.

### Instructions for Use

Phenylephrine has a rapid onset and short duration of action.

### Patient Monitoring and Laboratory Tests

When administered intravenously, monitor blood pressure and heart rate.

### Formulations

- Phenylephrine is available in 10-mg/mL injection, 1% nasal solution, and 2.5% and 10% ophthalmic solutions.

### Stability and Storage

Phenylephrine is soluble in water and may be mixed in IV solutions. It is also soluble in ethanol. It is subject to oxidation and will turn a darker color in some solutions, especially alkaline solutions. Discard formulations that turn a dark color. Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 10 mcg/kg (0.01 mg/kg) q15min IV as needed or 0.1 mg/kg q15min IM or SQ.
- CRI: 10 mcg/kg (0.01 mg/kg) IV, followed by 3 mcg/kg/min IV.

### Large Animal Dosage

- Horses: Dilute 10-20 mg in 500 mL of 0.9% saline solution and infuse over 10-15 minutes. Treatment of nephrosplenic entrapment is controversial.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 3

## Phenylpropanolamine Hydrochloride

fen-ill-proe-pah-nole'ah-meen hye-droe-klor'ide

**Trade and other names:** PPA, Proin, UriCon, and Propalin (veterinary preparations)

**Functional classification:** Adrenergic agonist

## Pharmacology and Mechanism of Action

Adrenergic agonist. Sympathomimetic. Phenylpropanolamine nonselectively acts as an agonist for the alpha-adrenergic and beta-adrenergic receptor. These receptors are found throughout the body, such as on sphincters, blood vessels, smooth muscle, and heart. The most profound effects observed with phenylpropanolamine are on vascular smooth muscle (vasoconstriction) and urethral smooth muscle (increased tone of urethra). The half-life in dogs is 4-7 hours. However, the duration of effect may be at least 8-12 hours and as long as 24 hours in some animals. A longer interval of administration may prevent some downregulation of alpha-receptors.

## Indications and Clinical Uses

Phenylpropanolamine (PPA) has been used as a decongestant, as a mild bronchodilator, and to increase tone of the urinary sphincter. Pseudoephedrine and ephedrine are related drugs that produce similar alpha-receptor and beta-receptor effects. The most common use in animals is for treating urinary incontinence. The mechanism for this action appears to be via stimulating receptors on the sphincter. It has also been used to treat priapism (persistent erection) in dogs. Abuse potential and adverse effects have limited the routine use as a decongestant and appetite suppressant in human medicine. Most of the human preparations have been removed from the market, and the only forms readily available are those marketed for veterinary medicine.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects are attributed to excess stimulation of adrenergic (alpha and beta) receptors. Side effects include tachycardia (or bradycardia), cardiac effects, CNS excitement, restlessness, and appetite suppression. There are reports of adverse effects caused by PPA in people. In particular, it has caused problems with blood pressure and increased risk of strokes. Such a concern should also apply to animals, but there have been no specific reports of these problems in animals. In animals exposed to high doses (accidental ingestion), it produced agitation, vomiting, mydriasis, tremors, panting and cardiovascular effects. Prognosis is good following accidental exposure with supportive care.

### Contraindications and Precautions

Use cautiously in any animal with cardiovascular disease. Phenylpropanolamine has been abused by people and used as a recreational drug.

### Drug Interactions

Phenylpropanolamine and other sympathomimetic drugs can cause increased vasoconstriction and changes in heart rate. Use cautiously with other vasoactive drugs and alpha<sub>2</sub>-agonists such as dexmedetomidine and xylazine. Use cautiously with other drugs that may lower seizure threshold. Use of inhalant anesthetics with PPA may increase cardiovascular risk. Do not use with tricyclic antidepressants (TCA) or monoamine oxidase inhibitors (MAOI). However, studies in dogs have shown that although selegiline is a MAOI, it can be administered safely with phenylpropanolamine.

## Instructions for Use

Although frequency of administration has been every 8-12 hours in most cases, there is evidence that an interval of every 24 hours in dogs at a dose of 1.5 mg/kg is just as effective. In some animals, pseudoephedrine has been substituted for PPA with good success.

## Patient Monitoring and Laboratory Tests

Monitor heart rate and blood pressure in animals receiving treatment. Animals with urinary incontinence should be checked periodically for presence of UTIs.

### **Formulations**

- Phenyflpropanolamine is available in 25-, 50-, and 75-mg flavored tablets; 25-mg vanilla-flavored liquid, and 50-mg scored tablets (veterinary preparations). Human formulations of 15-, 25-, 30-, and 50-mg tablets are no longer available.

### **Stability and Storage**

The stability and potency of compounded formulations has not been evaluated.

### **Small Animal Dosage**

#### **Dogs**

- 1 mg/kg q8h PO. Increase dose to 1.5-2 mg/kg q8h PO if necessary. In some animals it may be possible to decrease frequency to q12h or q24h PO.

#### **Cats**

- No dose has been determined. A dose of 1 mg/kg q12h PO has been used (extrapolated from the canine use), and the dose has been adjusted as needed.

### **Large Animal Dosage**

- No large animal dose is available.

### **Regulatory Information**

There are no formulations currently marketed in the US for human use because of abuse potential and adverse cardiovascular events.

RCI Classification: 3

## **Phenytoin, Phenytoin Sodium**

fen-ih-toe-in

**Trade and other names:** Dilantin

**Functional classification:** Anticonvulsant, antiarrhythmic

### **Pharmacology and Mechanism of Action**

Anticonvulsant. Depresses nerve conduction via blockade of sodium channels. Phenytoin is also classified as a Class I cardiac antiarrhythmic. In cardiac tissue, phenytoin increases the threshold for triggering ventricular arrhythmias. It also decreases conduction velocity and does not shorten the refractory period as much as lidocaine.

### **Indications and Clinical Uses**

Phenytoin is commonly used as an anticonvulsant in people, but it is not effective in dogs and not used in cats. In dogs, elimination is so rapid that dosing is impractical. Phenytoin is used in horses for treating ventricular arrhythmias, controlling myotonia, rhabdomyolysis, hyperkalemic periodic paresis, and stringhalt.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects include sedation, gingival hyperplasia, skin reactions, and CNS toxicity. In horses, at high doses recumbency and excitement have been observed. Sedation in horses may be an initial sign of high plasma concentrations. Monitoring plasma concentrations in horses can prevent adverse effects.

#### **Contraindications and Precautions**

Do not administer to pregnant animals.

### Drug Interactions

Phenytoin will interact with drugs undergoing hepatic metabolism. Phenytoin is a potent cytochrome P450 enzyme inducer. When used with cytochrome P450 inhibitors, increased levels of phenytoin may occur.

### Instructions for Use

Because of short half-life and poor efficacy in dogs, other anticonvulsants are used as the first choice before phenytoin. Although there are questions of safety in cats, and little documented use, there are anecdotal accounts of successful use of phenytoin in cats for some neurological problems.

### Patient Monitoring and Laboratory Tests

Therapeutic drug monitoring can be performed; however, therapeutic concentrations have not been established for dogs and cats. In horses, effective plasma concentrations are 5-20 mcg/mL (average 8.8 mcg/mL). Therapy should be aimed at producing concentrations above 5 mcg/mL in horses.

### Formulations

- Phenytoin is available in 25-mg/mL oral suspension, 30- and 100-mg capsules (sodium salt), 50 mg/mL injection (sodium salt), and 50-mg chewable tablets.

### Stability and Storage

Store protected from light at room temperature. Phenytoin sodium will absorb carbon dioxide and must be kept in a tight container. Phenytoin is practically insoluble in water, but phenytoin sodium has a solubility of 15 mg/mL. It is soluble in ethanol and propylene glycol. pH of phenytoin is 10-12, and it may not be compatible with acidic solutions. It may precipitate from solution if mixed with solutions at a lower pH. Protect from freezing.

### Small Animal Dosage

#### Dogs

- Anticonvulsant: 20-35 mg/kg q8h.
- Antiarrhythmic: 30 mg/kg q8h PO or 10 mg/kg IV over 5 min.

#### Cats

- Safe and effective dose has not been established in cats.

### Large Animal Dosage

#### Horses

- Initial bolus of 20 mg/kg q12h PO for four doses, followed by 10-15 mg/kg q12h PO. A single IV dose in horses of 7.5-8.8 mg/kg can be used followed by oral maintenance doses.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 4

## Physostigmine

fye-zoe-stig'meen

**Trade and other names:** Antilirium

**Functional classification:** Anticholinesterase

**Pharmacology and Mechanism of Action**

Cholinesterase inhibitor. Anticholinesterase drug. This drug inhibits the enzyme that breaks down acetylcholine. Therefore it prolongs the action of acetylcholine at the synapse. The major difference between physostigmine and neostigmine or pyridostigmine is that physostigmine crosses the blood–brain barrier, and the others do not.

**Indications and Clinical Uses**

Physostigmine is used as an antidote for anticholinergic intoxication and as a treatment (antidote) for neuromuscular blockade. It has also been used as a treatment of ileus and urinary retention (such as postoperative urine retention) by increasing the tone of the bladder smooth muscle.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects caused by the cholinergic action result from inhibition of cholinesterase. These effects can be seen in the gastrointestinal tract as diarrhea and increased secretions. Other adverse effects can include miosis, bradycardia, muscle twitching or weakness, and constriction of bronchi and ureters. Adverse effects can be treated with anticholinergic drugs such as atropine.

**Contraindications and Precautions**

Do not administer with choline esters such as bethanechol.

**Drug Interactions**

Do not administer with other drugs that produce cholinergic effects.

**Instructions for Use**

Physostigmine is indicated primarily only for treatment of intoxication. If longer-term or routine systemic use of an anticholinesterase drug is needed, neostigmine and pyridostigmine are used because they have fewer adverse effects. When used, frequency of dose may be increased based on observation of effects.

**Patient Monitoring and Laboratory Tests**

Monitor heart rate and rhythm and gastrointestinal signs.

**Formulations**

- Physostigmine is available in a 1-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats**

- 0.02 mg/kg q12h IV.

**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 3

## Phytonadione

fye-toe-nah-dye'one

**Trade and other names:** AquaMephyton, Mephyton, Veta-K1, vitamin K<sub>1</sub>, phylloquinone, and phytonadione

**Functional classification:** Vitamin

### Pharmacology and Mechanism of Action

Vitamin K supplement. Phytonadione and phytonadione are synthetic lipid-soluble forms of vitamin K<sub>1</sub>. (Phytonadione is the British spelling of phytonadione.) Menadiol is vitamin K<sub>4</sub>, which is a water-soluble derivative converted in the body to vitamin K<sub>3</sub> (menadione).

Vitamin K<sub>1</sub> is a fat-soluble vitamin used to treat coagulopathies caused by anticoagulant toxicosis (warfarin or other rodenticides). These anticoagulants deplete vitamin K in the body, which is essential for synthesis of clotting factors. Administration of vitamin K in its various formulations can be used to reverse the effect of anticoagulant toxicity.

### Indications and Clinical Uses

Phytonadione is used to treat coagulopathies caused by anticoagulant toxicosis (warfarin or other rodenticides). In large animals, it is used to treat sweet clover poisoning.

### Precautionary Information

#### Adverse Reactions and Side Effects

In people, a rare hypersensitivity-like reaction has been observed after rapid IV injection. Signs resemble anaphylactic shock. These signs also have been observed in animals. To avoid anaphylactic reactions, do not administer intravenously.

#### Contraindications and Precautions

Accurate diagnosis to rule out other causes of bleeding is suggested. Other forms of vitamin K may not be as rapidly acting as vitamin K<sub>1</sub>; therefore consider using a specific preparation. To avoid anaphylactic reactions, do not administer intravenously.

#### Drug Interactions

No drug interactions are reported.

### Instructions for Use

Consult poison control center for specific protocol if specific rodenticide is identified. Use vitamin K<sub>1</sub> for acute therapy of toxicity because it is more highly bioavailable. Administer with food to enhance oral absorption. If an injection is used, it can be diluted in 5% dextrose or 0.9% saline but not other solutions. The preferred injectable route is SQ, but IM can also be used. Although vitamin K<sub>1</sub> veterinary labels have listed the IV route for administration, these labels have not been approved by the FDA. Therefore avoid IV administration of vitamin K<sub>1</sub>.

### Patient Monitoring and Laboratory Tests

Monitoring bleeding times in patients is essential for accurate dosing of vitamin K<sub>1</sub> preparations. When treating long-acting rodenticide poisoning, periodic monitoring of the bleeding times is suggested.

### Formulations

- Phytonadione is available in 5-mg tablets (Mephyton) and 25-mg capsules (Veta-K1).
- Phytonadione (AquaMephyton) is available in a 2- or 10-mg/mL injection.



## Stability and Storage

Store in a tightly sealed container at room temperature. It is light sensitive and should be protected from light. Phytanadione is practically insoluble in water. However, it is soluble in oils and slightly soluble in ethanol. Do not mix with aqueous solutions. If mixed as a suspension for oral use, administer soon after preparation. Do not freeze.

## Small Animal Dosage

### Dogs and Cats

- Treatment of short-acting rodenticides: 1 mg/kg/day for 10-14 days, SQ, or PO.
- Treatment of long-acting rodenticides: 2.5-5 mg/kg/day for 3-4 weeks IM, SQ, or PO.

### Birds

- 2.5-5 mg/kg q24h.

## Large Animal Dosage

### Cattle, Calves, Horses, Sheep, and Goats

- 0.5-2.5 mg/kg SQ or IM.

## Regulatory Information

Withdrawal times are not established for animals that produce food. It is anticipated that milk and meat withdrawal times will be short. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Pimobendan

pim-oh-ben'dan

**Trade and other names:** Vetmedin

**Functional classification:** Cardiac inotropic agent

## Pharmacology and Mechanism of Action

Pimobendan is both a positive inotrope and a vasodilator. The vasodilator effects occur via inhibition of Phosphodiesterase III (PDE III). Phosphodiesterase III is the enzyme that degrades cyclic adenosine monophosphate (cAMP); therefore its action is to increase intracellular concentrations of cAMP. There may be some inhibition of PDE V in the pulmonary circulation. The inotropic effects of pimobendan are attributed to its action as a calcium sensitizer rather than the PDE inhibition. By acting as a calcium sensitizer, it increases the interaction of troponin C with contractile proteins and acts as an inotropic agent. The benefits in heart failure are caused by both positive inotropic effects and vasodilating properties. Other beneficial effects may include anti-inflammatory activity, increased sensitivity of baroreceptors, increased lusitropy, and decreased platelet aggregation. The cardiovascular effects occur after 1 hour and persist for 8-12 hours after administration. Pimobendan is absorbed best in an acidic environment. Fluctuating pH conditions in stomach and administration with food may produce inconsistent oral absorption.

In cats, pimobendan produces much higher blood concentrations than dogs and the half-life is almost three times longer than in dogs. Pimobendan is metabolized (demethylated) to desmethylpimobendan (DMP), which is an active metabolite with greater effect on PDE III activity. Both pimobendan and DMP are calcium sensitizers, but cats are less responsive to DMP than dogs.

## Indications and Clinical Uses

Pimobendan is indicated for use in dogs for treatment of congestive heart failure (CHF). It has been used in dogs with either valvular insufficiency or cardiomyopathy. In dogs with heart failure caused by valvular disease, it decreased heart rate, decreased left ventricular and left atrial dimensions, and reduced preload and natriuretic peptide concentrations. It is considered by many cardiologists as an essential initial treatment for dilated cardiomyopathy in dogs. When used in dogs, it has improved signs of heart failure and increased survival. When used in dogs, it may be administered with diuretics (furosemide), spironolactone, and ACE inhibitors. Pimobendan treatment has produced significant improvement compared to placebo in dogs treated with an ACE inhibitor and a diuretic. Pimobendan also may be helpful for treating Doberman pinschers with occult (asymptomatic) dilated cardiomyopathy by prolonging onset of clinical signs, improving survival and overall outcome.

It has not been recommended to administer positive inotropic agents such as pimobendan to cats with hypertrophic cardiomyopathy. However, it has been associated with improvement in clinical signs and longer survival time in cats with heart failure associated with dilated cardiomyopathy as part of a therapeutic regimen that may include other drugs (e.g., furosemide). When administered at 1.25 mg/cat q12h (0.25 mg/kg), it has been well tolerated.

## Precautionary Information

### Adverse Reactions and Side Effects

Pimobendan is potentially arrhythmogenic, but this effect (e.g., atrial fibrillation or ventricular arrhythmias) has been rare and seen primarily in animals with severe underlying cardiac disease. At doses of 0.25–0.5 mg/kg in dogs, pimobendan did not activate the renin–angiotensin–aldosterone system (RAAS), but if furosemide is added to treatment, some activation of the RAAS may occur. At therapeutic doses, there has been negligible effect on platelet aggregation.

### Contraindications and Precautions

Use cautiously in animals prone to cardiac arrhythmias. Do not use in animals with obstructive cardiomyopathy or a fixed obstruction of the outflow tract. Compounded formulations will not achieve the same absorption profile in dogs as the proprietary form. There is a critical pH at which the oral absorption is enhanced, and some compounded formulations may lack excipients to attain this effect.

### Drug Interactions

Use cautiously with other PDE inhibitors such as theophylline, pentoxifylline, and sildenafil (Viagra) and related drugs. Sildenafil is a PDE V inhibitor; theophylline is a PDE IV inhibitor. Pimobendan is insoluble unless in an acidic environment, and it is difficult to mix pimobendan into a solution.

## Instructions for Use

Follow label instruction for use. Evaluate stage of heart failure in animals before use. Consider the addition of other drugs such as ACE inhibitors, spironolactone, furosemide, and digoxin in animals as the severity of the heart disease increases. If furosemide is used concurrently with pimobendan, consider the addition of an ACE inhibitor (e.g., enalapril, benazepril) or aldosterone antagonist (e.g., spironolactone) to inhibit RAAS activation.

## Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and rhythm during use.

**Formulations**

- Pimobendan is available in chewable tablets of 1.25, 2.5 and 5 mg. In Europe, pimobendan is available in 2.5- and 5-mg capsules.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Acidic pH conditions are important for the stability of the formulation and to ensure dissolution.

**Small Animal Dosage****Dogs**

- 0.25-0.3 mg/kg q12h PO.

**Cats**

- 1.25 mg/cat q12h PO (0.1-0.3 mg/kg q12h).

**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

Do not administer to animals intended for food.

**Piperacillin Sodium and Tazobactam**

pih'per-ah-sill'in soe'dee-um Taze'oh back tam

**Trade and other names:** Zosyn and generic. Also referred to as "Pip-Taz."

**Functional classification:** Antibacterial, beta-lactam

**Pharmacology and Mechanism of Action**

Beta-lactam antibiotic of the acylureidopenicillin class. Like other beta-lactams, piperacillin binds PBPs that weaken or interfere with cell wall formation. After binding to PBPs, the cell wall weakens or undergoes lysis. Like other beta-lactams, this drug acts in a time-dependent manner (i.e., it is more effective when drug concentrations are maintained above the MIC values during the dose interval). Compared to other beta-lactam antibiotics, piperacillin has good activity against *Pseudomonas aeruginosa*. It also has good activity against streptococci, but is not active against methicillin-resistant *Staphylococcus*. Piperacillin has a short half-life in animals and must be given by injection (usually IV), which limits its usefulness. Tazobactam is a beta-lactamase inhibitor. When administered in combination with piperacillin, it increases the spectrum to include beta-lactamase-producing strains of gram-negative and gram-positive bacteria.

**Indications and Clinical Uses**

Piperacillin has similar activity as ampicillin, but it is extended to include many organisms that otherwise are resistant to ampicillin, such as *P. aeruginosa* and other gram-negative bacilli. The in vitro activity against some gram-negative bacteria is enhanced when administered with an aminoglycoside (e.g., gentamicin or amikacin). The addition of tazobactam further increases the spectrum to include beta-lactamase-producing strains.

The use includes septicemia, UTIs, skin, soft tissue, respiratory infections, and intraabdominal infections. Targeted organisms include bacteria of the Enterobacteriaceae spp. (*Escherichia coli*, *Klebsiella pneumoniae*) and *P. aeruginosa*.

In veterinary medicine, other penicillin-beta-lactamase inhibitor combinations have been ampicillin and sulbactam (Unasyn) and ticarcillin and clavulanate.

However, ampicillin and sulbactam's spectrum of coverage often does not include many of the gram-negative bacteria encountered. Ticarcillin and clavulanate, once a popular injectable antibiotic in veterinary medicine, is no longer available. Therefore piperacillin and tazobactam is a logical substitute as a penicillin–beta-lactamase inhibitor combination for in-hospital veterinary use. Pharmacokinetic data for dogs indicate a half-life of 0.55 hours, a volume of distribution of 0.27 L/kg, and clearance of 5.79 mL/kg/minute. Protein binding in dogs is 18%.

### Precautionary Information

#### Adverse Reactions and Side Effects

Allergy to penicillin is the most common adverse effect. High doses may inhibit platelet function.

#### Contraindications and Precautions

Do not use in patients allergic to penicillin drugs. High doses contribute to the sodium load in a patient.

#### Drug Interactions

Do not mix in vials or syringes with other drugs.

### Instructions for Use

Piperacillin is combined with tazobactam (beta-lactamase inhibitor) in Zosyn, which increases the spectrum to include beta-lactamase-producing strains of *Staphylococcus* and gram-negative bacteria. Ticarcillin-clavulanate has a similar spectrum of activity but is no longer available. Piperacillin-tazobactam has a more active spectrum of activity against gram-negative bacteria than ampicillin-sulbactam.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break points for susceptible organisms are  $\leq 8$  mcg/mL (piperacillin/tazobactam).

### Formulations

- Piperacillin and tazobactam are typically in 8:1 ratio of piperacillin:tazobactam. It is available in vials containing 2 grams piperacillin and 0.25 grams tazobactam, 3 grams piperacillin and 0.375 grams tazobactam, or 4 grams piperacillin and 0.5 grams tazobactam. Vials are reconstituted with sterile water, 0.9% saline solution, or 5% dextrose in water and further diluted to desired volume for IV fluid administration.

### Stability and Storage

Reconstituted solution should be used within 24 hours or 7 days if refrigerated.

### Small Animal Dosage

#### Dogs and Cats

- 50 mg/kg q6h IV or IM. Alternatively, a constant rate infusion (CRI) can be administered by injecting a loading dose of 4 mg/kg (bolus), followed by 3.2 mg/kg/hour.

### Large Animal Dosage

- No doses have been reported for large animals, but doses similar to those cited for ticarcillin-clavulanate would likely reach the same targets in horses.

### Regulatory Information

Withdrawal times are not established for animals that produce food. However, because of rapid elimination, it is anticipated that withdrawal times will be similar to that of other beta-lactams such as ampicillin.

## 642 Piperazine

For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

### Piperazine

pih-peer'e-zeen

**Trade and other names:** Pipa-Tabs and generic brands

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Antiparasitic compound. Piperazine produces neuromuscular blockade in parasites through selective antagonism of GABA receptors, resulting in opening of chloride channels, hyperpolarization of parasite membrane, and paralysis of worms. Efficacy is limited primarily to roundworms. In horses, it is active against small strongyles and roundworms.

### Indications and Clinical Uses

Piperazine is a common antiparasitic drug and is widely available, even over-the-counter (OTC). It is used primarily for treatment of roundworm (ascarid) infections in animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Piperazine is remarkably safe in all species but can cause ataxia, muscle tremors, and changes in behavior.

#### Contraindications and Precautions

No contraindications in animals. It may be used in all ages.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Piperazine is a widely used antiparasitic drug with a wide margin of safety. It may be used in combination with other antiparasitic drugs.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Piperazine is available in an 860-mg powder; 140-mg capsules; 50- and 250-mg tablets; and 128-, 160-, 170-, 340-, 510-, and 800-mg/mL oral solution.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 44-66 mg/kg administered once PO.

## Large Animal Dosage

### Horses and Pigs

- 110 mg/kg PO in the drinking water as the sole water source.
- Oral solution (horses): 30 mL (1 ounce) of 17% piperazine solution administered PO for each 45 kg of body weight.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Piroxicam

peer-oks'ih-kam

**Trade and other names:** Feldene and generic brands

**Functional classification:** Nonsteroidal anti-inflammatory drug

## Pharmacology and Mechanism of Action

Piroxicam is an NSAID of the oxicam class. Clinical effects are similar to other NSAIDs (see meloxicam). These drugs have analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAIDs is the COX enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy gastrointestinal tract, renal function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects and COX-2 activity is important for some biological effects. Piroxicam, using in vitro assays, is somewhat more selective for COX-2 than COX-1. In animals, it is not certain that the specificity for COX-1 or COX-2 is related to efficacy or safety. Piroxicam also may have some anti-tumor or tumor-preventative effects and is used in some anticancer protocols. Piroxicam has a longer half-life than other NSAIDs in dogs, with a half-life of 35-40 hours and near 100% oral absorption. The half-life is shorter in other species, with a half-life in cats of 13 hours and average oral absorption of 89% and a half-life in horses of 3-4 hours.

## Indications and Clinical Uses

Piroxicam is primarily used to treat pain and inflammation associated with arthritis and other musculoskeletal conditions. It is not used as much for these conditions as other approved NSAIDs for animals. Another use in dogs and cats has been as an adjunct for treating cancer. This use is based on reports of its activity for treating or suppressing some tumors, including transitional cell carcinoma of the bladder, squamous cell carcinoma, and mammary adenocarcinoma. (This effect is not unique to piroxicam, as other NSAIDs also may have antitumor properties.) Piroxicam has been used in combination with cisplatin to treat oral malignant melanoma and oral squamous cell carcinoma in dogs (0.3 mg/kg).

## Precautionary Information

### Adverse Reactions and Side Effects

Elimination of piroxicam is slow. At 0.3 mg/kg q24h PO, adverse reactions have been observed in dogs, and an administration interval of every 48 hours should be considered. Adverse effects are primarily gastrointestinal toxicity (e.g., gastric ulcers). Renal toxicity also is a risk, especially in animals prone to dehydration or that have compromised renal function. Toxic epidermal necrolysis has been reported in some dogs.

In cats, vomiting is possible during initial treatment for long-term management of some cancers. Long-term treatment was not associated with hematologic, renal, or liver toxicity in cats.

### Contraindications and Precautions

Use cautiously in dogs because the long half-life may increase risk of gastrointestinal ulcers if administered once daily. The human formulation is too large a dose for most dogs and should be reformulated to avoid overdose. Warn pet owners about overdoses that could produce gastrointestinal ulceration. Do not administer to animals prone to gastrointestinal ulcers. Do not administer to pregnant animals. Use cautiously in animals with kidney disease that may be prone to dehydration, or if administered with other drugs that may injure the kidney, such as cisplatin.

### Drug Interactions

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the gastrointestinal adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and ACE inhibitors.

## Instructions for Use

Most experience with dosing has been accumulated from studies in which dogs were treated with piroxicam for transitional cell carcinoma of the bladder. Some of these dogs tolerated piroxicam better with respect to gastrointestinal toxicity if the drug was administered with misoprostol. Piroxicam has also been used in dogs for treatment of squamous cell carcinoma.

## Patient Monitoring and Laboratory Tests

Piroxicam has the potential of inducing gastrointestinal ulceration. Monitor for signs of vomiting, bleeding, and lethargy. If bleeding is suspected, monitor patient's hematocrit or CBC. Monitor renal function in treated animals.

## Formulations

- Piroxicam is available in 10-mg capsules.

## Stability and Storage

Exposure to light results in photodegradation. Piroxicam is only slightly soluble in water. It is soluble in basic solutions and some organic solvents. Compounded formulations made for small animals may be stable for only 48 hours. Although an IV formulation is not available commercially, a 2-mg/mL solution has been prepared from mixing the pure powder with 0.1 N NaOH and found to be stable if stored in a glass vial, refrigerated, and protected from light.

## Small Animal Dosage

### Dogs

- 0.3 mg/kg q48h PO.
- Cancer treatment: Dogs also have tolerated 0.3 mg/kg q24h PO.

**Cats**

- 0.3 mg/kg q24h PO. A common dose is 1 mg per cat q24h PO.

**Large Animal Dosage**

There is insufficient evidence to recommend doses for large animals. Single doses of 0.2 mg/kg PO have been administered to horses without any adverse effects.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).  
RCI Classification: 4

**Plicamycin**

plye-kah-mye'sin

**Trade and other names:** Mithracin and Mithramycin

**Functional classification:** Anticancer agent

**Pharmacology and Mechanism of Action**

Anticancer agent. The action of plicamycin is to complex with DNA in the presence of divalent cations and inhibit DNA and RNA synthesis. It lowers serum calcium and may have direct action on osteoclasts to decrease serum calcium.

**Indications and Clinical Uses**

Plicamycin is used in cancer protocols for carcinomas and treatment of hypercalcemia. Use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects have not been reported in animals. In people, hypocalcemia and gastrointestinal toxicity have been reported. Plicamycin may cause bleeding problems.

**Contraindications and Precautions**

Do not use with drugs that may increase the risk of bleeding (e.g., NSAIDs, heparin, or anticoagulants).

**Drug Interactions**

No drug interactions have been reported.

**Instructions for Use**

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

**Patient Monitoring and Laboratory Tests**

Monitor serum calcium concentrations.

**Formulations**

- Plicamycin is available in a 2.5-mg vial for injection and 0.5 mg/mL when diluted.



## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- Antihypercalcemic: 25 mcg/kg/day IV (slow infusion) over 4 hours.
- Antineoplastic (dogs): 25-30 mcg/kg/day IV (slow infusion) for 8-10 days.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Polyethylene Glycol Electrolyte Solution

pahl-ee-eth'ill-een glye'kole

**Trade and other names:** GoLYTELY, PEG, Colyte, and Co-Lav

**Functional classification:** Laxative

## Pharmacology and Mechanism of Action

Saline cathartic. Polyethylene glycol electrolyte solution is a nonabsorbable compound that increases water secretion into the bowel via osmotic effect. These isosmotic liquids pass through the bowel without absorption. Oral administration produces a profound cathartic effect.

## Indications and Clinical Uses

Polyethylene glycol electrolyte solution is a cathartic that is used primarily for evacuating the bowel and cleansing of the intestine prior to endoscopy and surgical procedures. It is administered PO and will induce a rapid osmotic cathartic effect. It is effective for bowel cleansing, but it requires high volumes to be effective. In some human patients, smaller volumes can be used if it is combined with another laxative, such as bisacodyl.

## Precautionary Information

### Adverse Reactions and Side Effects

Water and electrolyte loss with high doses or prolonged use are common. Large volumes required may cause nausea.

### Contraindications and Precautions

Do not administer to animals that are dehydrated because it may cause fluid and electrolyte loss. It is not indicated for chronic use.

### Drug Interactions

No specific drug interactions.

## Instructions for Use

Used for bowel evacuation prior to surgical or diagnostic procedures. Large volumes are required. In human patients, administration of only half the volume can be used

if taken with bisacodyl (one to four tablets) 2 hours prior to procedure. This combination is called HalfLyte.

### Patient Monitoring and Laboratory Tests

Monitor electrolytes if it is administered repeatedly.

### Formulations

- Polyethylene glycol electrolyte is an oral solution. Preparations contain PEG 3350, sodium chloride, potassium chloride, sodium bicarbonate, and sodium sulfate.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 25 mL/kg PO, repeat in 2-4 hours.

### Large Animal Dosage

#### Horses and Cattle

- Via stomach tube: 500 mL to 4 L once PO.

### Regulatory Information

No withdrawal times necessary.

## Polymyxin B Sulfate

poly mix-in bee

**Trade and other names:** Generic

**Functional classification:** Antibacterial agent

### Pharmacology and Mechanism of Action

Antibiotic, antibacterial agent. Polymyxin B is from a group of polypeptide antibiotics. Polymyxins are basic surface-active cationic detergents that interact with the phospholipid within the cell membrane. They are capable of penetrating the cell membrane of bacteria and disrupting the structure. This action subsequently induces permeability changes within the cell that result in cell death, giving polymyxins bactericidal properties. Polymyxin B is capable of acting as a chelating agent to bind the lipid A portion of endotoxin in a 1:1 ratio to neutralize lipopolysaccharide (LPS).

Polymyxins contain seven amino acids in a cyclic configuration and have a molecular weight of more than 1000. Other polymyxins have been named A, B, C, D, E, and M, but only B and E in their sulfate salt forms are used clinically. Polymyxin B sulfate is a mixture of polymyxin B1 and polymyxin B2. Polymyxin E is more commonly known as *colistin*, which is also used systemically for some infections that are resistant to other drugs. Polymyxin B has a pKa ranging from 8-9 derived from the organism *Bacillus polymyxa*. It is available in many topical formulations, often in formulations considered “triple antibiotics.” The injectable formulation of polymyxin B sulfate is a sulfate salt of two forms: polymyxins B1 and B2. It is available in formulations of not less than 6000 polymyxin B units per milligram (as the anhydrous base). Polymyxins are not absorbed from the gastrointestinal tract when administered orally, but are rapidly absorbed when given parenterally and have 70%-90% plasma protein binding.

## Indications and Clinical Uses

Polymyxin B for injection is in powder form suitable for preparation of sterile solutions for IM, IV drip, intrathecal, or ophthalmic use. Polymyxin B is most often administered as a topical ointment for managing infections. It is one of the components of “triple antibiotic” ointments used for topical use. Systemically, polymyxin has been used to treat infections that are resistant to other drugs. Bacteria such as *Pseudomonas aeruginosa* and *Acinetobacter* may develop resistance to other drugs that can be treated only with drugs such as colistin and polymyxin. In people, polymyxin B is used to treat UTI, meningitis, and septicemia. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness in animals for treating bacterial infections. In veterinary medicine—particularly horses—polymyxin has been used because of its property to bind to the lipid A portion of bacterial endotoxin in the blood and prevent signs of bacterial septicemia without producing kidney injury. Infusions ranging from 1000 to 10,000 units per kg (a common dose is 6000 units/kg, equivalent to 1 mg/kg) administered every 8 hours have been shown to be safe and effective for treating endotoxemia in horses. The action is attributed to the cationic portion of polymyxin B binding to the anionic lipid A portion of this endotoxin. This effectively renders the endotoxin inactive, thereby preventing most of the adverse effects attributed to gram-negative endotoxin. This effect also has been demonstrated in an experimental model of feline endotoxemia in which it had antiendotoxin effects in vivo.

## Precautionary Information

### Adverse Reactions and Side Effects

Intramuscular injections will cause pain. Because of its ability to bind to phospholipid membranes and cause injury, the most severe adverse reaction is caused by renal injury. Kidney injury is a dose-dependent problem caused by increased membrane permeability and influx of cations, anions, and water, causing kidney cell swelling. However, at doses that have been used for treating endotoxemia (6000 units/kg, IV every 8 hours), it has not caused kidney injury in horses. At the dose used for treating bacterial endotoxemia in horses, kidney injury has not been observed. However, at higher doses (18,000–36,000 units/kg) or for longer treatment protocols, renal injury risk increases. Allergic reactions are also possible. At high doses administered intravenously to cats (3 mg/kg and higher), it produced respiratory depression.

### Contraindications and Precautions

Use cautiously, if at all, in patients with renal disease. Animals receiving polymyxin B should receive adequate fluid support to maintain hydration and renal perfusion.

### Drug Interactions

Use cautiously with other potentially nephrotoxic agents such as aminoglycosides. Do not administer with curariform muscle relaxant and other neurotoxic drugs because of risk of respiratory depression. Polymyxin antibacterial activity is decreased in the presence of pus, in tissues containing acidic phospholipids, and in the presence of anionic detergents.

## Instructions for Use

Use in veterinary medicine has been primarily confined to topical use and the use in horses to treat endotoxemia. Doses and regimens have been derived from experimental studies. Routes of administration have been topical IM, IV infusion, intrathecal, or ophthalmic.

## Patient Monitoring and Laboratory Tests

Monitor patient hydration and electrolyte status. Monitor renal parameters (e.g., creatinine and BUN) for evidence of renal disease.

## Formulations

- Polymyxin B is available in vials containing 500,000 polymyxin B units. In some dosage protocols, the dose is listed in milligrams instead of units. One milligram of polymyxin B base is equivalent to 10,000 units of polymyxin B, and each microgram of pure polymyxin B base is equivalent to 10 units of polymyxin B.

## Stability and Storage

Store at room temperature 20° C to 25° C (68° F to 77° F), protected from light. Polymyxin B is soluble in water at 0.5% solution with a pH of 5-7.5. Aqueous solutions of polymyxin B sulfate have been stored up to 12 months without significant loss of potency if refrigerated. Do not mix with strong acid or alkaline solutions. It is not compatible with calcium or magnesium salts.

## Small Animal Dosage

### Dogs and Cats

- Antibacterial: 15,000-25,000 units/kg q12h IV. To prepare solution, mix 500,000 polymyxin B units with 300-500 mL 5% dextrose for CRI.
- Antibacterial: 30,000 units/kg/day IM. To prepare solution, mix 500,000 polymyxin B units in 2 mL sterile water for injection or sodium chloride injection or 1% procaine hydrochloride.
- Antitendotoxin: 1 mg/kg diluted in 10 mL of 0.9% saline solution given as an IV infusion.
- Intrathecal (to treat meningitis): Mix 500,000 polymyxin B units in 10 mL sodium chloride (50,000 units per mL). Administer 20,000 units once daily intrathecally, then continue 25,000 units once every other day.

## Large Animal Dosage

Horses (endotoxemia): 1000-10,000 units per kg (usually 6000 units/kg, equivalent to 1 mg/kg) administered every 8 hours. The repeat treatments may be necessary if there is ongoing sepsis. The infusion may be mixed in a 1-L saline solution and administered over 15 minutes every 8 hours for five treatments.

## Regulatory Information

Cattle: Withdrawal time after intramammary administration is 7 days for milk and 2 days for meat. Other withdrawal times have not been reported for food animals. For other extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Polysulfated Glycosaminoglycan

pahl-ee-sul'fate-ed glye-koe-sah-mee-noe-glye-kan

**Trade and other names:** Adequan Canine, Adequan IA, and Adequan IM

**Functional classification:** Antiarthritic agent

## Pharmacology and Mechanism of Action

Polysulfated glycosaminoglycan (PSGAG) provides large-molecular-weight compounds similar to normal constituents of healthy joints. It is chondroprotective and inhibits

## 650 Polysulfated Glycosaminoglycan

enzymes that may degrade articular cartilage, such as metalloproteinase. It may help to upregulate glycosaminoglycan and collagen synthesis and decrease inflammatory mediators (e.g., PGE<sub>2</sub>).

### Indications and Clinical Uses

PSGAG is injected in dogs and horses to treat or prevent degenerative joint disease. Intraarticular injections have been effective, but intramuscular doses may be too low to be effective in some animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are rare. Allergic reactions are possible. PSGAG has heparin-like effects and may elicit bleeding problems in some animals, but this has not been observed clinically.

#### Contraindications and Precautions

Intraarticular injections should be done using aseptic technique. Use cautiously in animals receiving heparin therapy.

#### Drug Interactions

No drug interactions are reported in animals.

### Instructions for Use

Doses are derived from empirical evidence, experimental studies, and clinical studies. Although effective for acute arthritis, it may not be as effective for chronic arthropathy. In horses, it is sometimes combined with amikacin (125 mg) for intraarticular use to prevent infection.

### Patient Monitoring and Laboratory Tests

Observe injected joints for signs of infection after treatment.

### Formulations

- Polysulfated glycosaminoglycan is available in a 100-mg/mL injection in a 5-mL vial, 100 mg/mL for IM administration, and 250 mg/mL for intraarticular use in horses.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 4.4 mg/kg IM, twice weekly for up to 4 weeks.

### Large Animal Dosage

#### Horses

- 500 mg every 4 days IM for 28 days or 250 mg per joint once weekly for 5 weeks intraarticular.

### Regulatory Information

No withdrawal times necessary.

## Ponazuril

poe-naz'yoo-ril

**Trade and other names:** Marquis

**Functional classification:** Antiprotozoal

### Pharmacology and Mechanism of Action

Antiprotozoal drug. Coccidiostat. Ponazuril (also known as toltrazuril sulfone) is a metabolite of the poultry antiprotozoal drug toltrazuril. Ponazuril is a triazine-based drug that acts to inhibit enzyme systems in protozoa and/or decreasing pyrimidine synthesis. It is specific for apicomplexan organisms because the action attacks the apicoplast organelle in protozoa. This action produces a specific effect as an antiprotozoal agent without affecting other organisms. It has high oral absorption in horses. The half-life data has been conflicting for horses with different studies reporting 1.6 days, 2.5 days, and 4.5 days. The half-life is 2.4 hours in cattle and 5.6 days in pigs. One week of daily dosing in horses is needed to reach steady-state concentrations. A level of 100 ng/mL is believed to be necessary to prevent and treat infections caused by *Sarcocystis neurona*.

### Indications and Clinical Uses

Toltrazuril, the parent drug, has been used for protozoa such as *Isospora*, *Coccidia* spp., *Toxoplasma gondii*, *Sarcocystis neurona*, and *Eimeria* spp. Ponazuril has a long half-life in horses, and concentrations in cerebrospinal fluid (CSF) are 3.5%-4% of serum concentrations but high enough to inhibit protozoa. Ponazuril is specifically approved for use as a treatment of equine protozoal myeloencephalitis (EPM), caused by *S. neurona*. In clinical studies in horses with EPM, 62% of 101 horses were treated successfully with doses of 5 or 10 mg/kg for 28 days. There is limited information available on its use in other animals, but some anecdotal accounts on the use for treating toxoplasmosis in cats and protozoa in other species. It has been used to treat piglets with diarrhea caused by *Isospora suis*.

### Precautionary Information

#### Adverse Reactions and Side Effects

Ponazuril is highly specific and relatively safe at approved doses. Administration of 50 mg/kg to horses (10 times the recommended dose) produced minor adverse effects. There were minimal changes in the serum analysis. Soft feces may occur at high doses.

#### Contraindications and Precautions

Avoid use in pregnant or breeding mares until more information becomes available on safety.

#### Drug Interactions

No drug interactions have been reported.

### Instructions for Use

Use in horses is based on clinical studies, field trials conducted by the drug sponsor, and pharmacokinetic studies in horses. In a trial with either 5 or 10 mg/kg per day in horses, 62% were improved by 28 days. Although successful treatment was reported after 28 days, longer treatment duration may be needed in some animals to resolve the infection and prevent relapse. There is only limited use of ponazuril in other animals and doses listed for other species (see dosing section) are based primarily on anecdotal reports.

## Patient Monitoring and Laboratory Tests

In horses treated for EPM, monitor neurologic status during treatment. The immunoglobulin G (IgG) and albumin quotient has been measured in CSF of treated horses to monitor treatment, but this may not indicate clinical cure.

## Formulations

- Ponazuril is available in 15% (150-mg/mL) oral paste for horses.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Cats

- Treatment of toxoplasmosis: 20 mg/kg PO q24h.
- Kittens (toxoplasmosis): 50 mg/kg once PO or 20 mg/kg once daily for 2 days PO.

### Dogs

- 10 mg/kg PO q12h.

## Large Animal Dosage

### Horses

- Treatment of EPM: 5 mg/kg q24h PO for 28 days. A loading dose of 15 mg/kg has been used initially (day 1) followed by maintenance daily doses for 28 days.

### Pigs

- 5 mg/kg, PO, for treatment of *Isospora suis*.

## Regulatory Information

Recommended withdrawal time for pigs is 33 days. Withdrawal times for other food animals is not available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Posaconazole

Poe-sa-Kon'-a-zole

**Trade and other names:** Noxafil

**Functional classification:** Antifungal

## Pharmacology and Mechanism of Action

Antifungal drug. Posaconazole is a relatively new antifungal of the azole group, similar to itraconazole in structure and activity. Action against fungi is similar to other azoles, which is to inhibit ergosterol synthesis in the fungal cell membrane and produce fungistatic activity. It is active against dermatophytes, *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Coccidioides immitis*, and *Cryptococcus neoformans*. The difference in activity compared to other azoles is the additional activity against other fungi. The spectrum includes *Fusarium* and Mucorales (formerly called Zygomycetes), such as *Mucor* and *Rhizopus*. Posaconazole's activity is superior to that of other antifungals against many clinically important organisms. Against many strains tested it was more active than itraconazole and fluconazole and more active than amphotericin B. It is active against fluconazole-resistant strains of *Candida* spp., dermatophytes and other opportunistic fungi, and more potent than fluconazole or itraconazole against *Aspergillus* spp. It has a higher safety margin, fewer drug interactions, and a narrower toxicity profile compared with characteristics of other antifungals.

In dogs, the half-life from oral administration of the liquid suspension is 24 hours and from the delayed-release tablet was 41.7 hours. After IV administration, the

half-life was 29 hours, with a volume of distribution of 3.3 L/kg. Oral absorption from the liquid suspension was 26%, but was much higher and with higher peak concentrations from the oral delayed-release tablet. Plasma protein binding in dogs, as in other species, was >99%. Studies in a small group of cats showed that it had a half-life of approximately 40 hours after oral dosing and oral bioavailability of 16%.

## Indications and Clinical Uses

The use of posaconazole has been limited to a few case reports and anecdotal experience. In cats, it has been used to treat fungal infections refractory to other drugs such as aspergillosis and *Mucor* infections. In humans, it is used for invasive fungal infections, including those caused by *Aspergillus* and *Candida*. It is also active against dermatophytes, *H. capsulatum*, *B. dermatitidis*, *C. immitis*, and *C. neoformans*. Its advantage over other azole drugs is the activity against *Fusarium* and *Mucorales* (formerly called Zygomycetes), such as *Mucor* and *Rhizopus*. The only formulations available for systemic use are the human products, which at this time, are quite expensive, which has discouraged routine use.

## Precautionary Information

### Adverse Reactions and Side Effects

The use has been relatively infrequent, and information regarding the full range of adverse effects possible from clinical use is not available. In people, similar adverse effects have been observed as with other azole antifungal drugs: headache, diarrhea, nausea, and increased liver enzymes, but there is some indication that the safety profile may be better than other azoles. In toxicity studies, dogs have tolerated 30 mg/kg/day for 1 year without any clinical signs. However, histologically some neuronal vacuolation was observed at this dose. It should not be used during pregnancy because of inhibition of steroidogenesis.

### Contraindications and Precautions

No contraindications and precautions have been reported for animals.

### Drug Interactions

Drugs that decrease stomach acid (PPIs, H<sub>2</sub> blockers) will reduce oral absorption of posaconazole. Like other azole antifungal drugs, posaconazole is a strong inhibitor of cytochrome P450 enzymes (CYP3A4) and may increase concentrations of other drugs metabolized by these enzymes.

## Instructions for Use

Use in animals has been based primarily on some isolated case reports (primarily in cats) and extrapolation from human use. Dosing recommendations are based on pharmacokinetic studies in dogs and cats. No clinical studies for animals have been reported. The oral absorption is enhanced when administered with food; therefore administer with a small meal. The injection can be administered as a loading dose in patients not amenable to oral treatment, but the injection formulation is very expensive.

## Patient Monitoring and Laboratory Tests

Monitor liver enzymes in treated animals. Although plasma concentrations are generally not measured, trough concentrations above 0.5–0.7 mcg/mL for mild infections or 1 mcg/mL for severe invasive infections are associated with efficacy.

## Formulations

- Posaconazole is available in a 40-mg/mL oral suspension, 100-mg delayed-release tablet, and 18-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.



## Small Animal Dosage

### Dogs

- Oral suspension: 10 mg/kg PO q24h.
- Oral delayed-release tablet: 5 mg/kg PO q48h.

### Cats

- For mild infections, or for preventative use, administer 15 mg/kg PO, followed by 8 mg/kg PO every 48 hours of the oral liquid suspension. For more severe invasive fungal infections, administer an oral loading dose of 30 mg/kg, followed by 15 mg/kg every other day, PO.

## Large Animal Dosage

- No doses have been reported.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Potassium Chloride

**Trade and other names:** Generic brands

**Functional classification:** Potassium supplement

## Pharmacology and Mechanism of Action

Potassium supplement. Potassium is used for treatment of hypokalemia. A dose 1.9 g of potassium chloride is equivalent to 1 g of potassium. One gram of potassium chloride is equal to 14 mEq of potassium. Other potassium supplements include potassium gluconate, potassium acetate, potassium bicarbonate, and potassium citrate.

## Indications and Clinical Uses

Potassium supplements are indicated for treating hypokalemia. Hypokalemia may occur with some diseases or as a consequence of diuretic use. Hypokalemia may also occur as a consequence of beta<sub>2</sub>-adrenergic agonist overdose. In most patients, potassium chloride is the supplement of choice for hypokalemia. It is better absorbed than other supplements, and the chloride ion may be helpful because hypochloremia may also occur in some patients.

## Precautionary Information

### Adverse Reactions and Side Effects

Toxicity from high potassium concentrations can be dangerous. Hyperkalemia can lead to cardiovascular toxicity (bradycardia and arrest) and muscular weakness. Oral potassium supplements can cause nausea and stomach irritation.

### Contraindications and Precautions

Do not exceed a rate of 0.5 mEq/kg/hr IV infusion. Use cautiously in animals with kidney disease. Do not use potassium chloride if metabolic acidosis and hyperchloremia are present. Use another potassium supplement instead. Intravenous use should be done cautiously because of risk of hyperkalemia. Use potassium cautiously in digitalized patients. Do not use with potassium penicillin or potassium bromide (use sodium salts of these drugs instead).

### Drug Interactions

Interactions between potassium supplements and the following drugs may occur: digoxin, thiazide diuretics, spironolactone, amphotericin B, corticosteroids, penicillins, ACE inhibitors, and laxatives.

### Instructions for Use

One gram of potassium chloride provides 13.41 mEq of potassium. It is usually added to fluid solutions. When potassium is supplemented in fluids, do not administer at a rate faster than 0.5 mEq/kg/hr.

### Patient Monitoring and Laboratory Tests

Monitor serum potassium levels. Monitor electrocardiogram (ECG) in patients that may be prone to arrhythmias. Normal potassium is 4-5.5 mEq/L (dogs) and 4.3-6.0 mEq/L (cats).

### Formulations

Potassium chloride is available in various concentrations for injection (usually 2 mEq/mL). It is available in an oral suspension and oral solution as 10-20 mEq of potassium per packet. One gram potassium chloride contains 14 mEq potassium ion.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Potassium chloride is freely soluble in water.

### Small Animal Dosage

#### Dogs and Cats

- Supplement: 0.5 mEq potassium/kg/day or add 10-40 mEq/500 mL of fluids, depending on serum potassium.
- Acute treatment of hypokalemia: 0.5 mEq potassium/kg/hr.

### Large Animal Dosage

#### Cattle and Horses

- Supplement in IV fluids to 20-40 mEq potassium per liter of fluids. Do not exceed a rate of 0.5 mEq/kg/hr IV.

### Regulatory Information

No withdrawal times necessary.

## Potassium Citrate

**Trade and other names:** Generic and Urocit-K

**Functional classification:** Alkalinizing agent

### Pharmacology and Mechanism of Action

Potassium citrate ( $K_3C_6H_5O_7$ ) alkalinizes urine and may increase urine citric acid. An increase in urine excretion of citrate and alkaline urine may decrease urinary calcium oxalate crystallization. Urinary excretion of calcium also is decreased. Other potassium supplements include potassium gluconate, potassium acetate, potassium bicarbonate, and potassium chloride.

### Indications and Clinical Uses

Potassium citrate is used for prevention of calcium oxalate urolithiasis. It is also used for renal tubular acidosis. In dogs, after administration of 150 mg/kg (of potassium citrate) q12h PO, the urine pH was not significantly increased, but urine concentration of calcium oxalate was decreased.

### Precautionary Information

#### Adverse Reactions and Side Effects

Toxicity from high potassium concentrations can be dangerous. Hyperkalemia can lead to cardiovascular toxicity (bradycardia and arrest) and muscular weakness. Oral potassium supplements can cause nausea and stomach irritation.

#### Contraindications and Precautions

Use cautiously in animals with kidney disease. Do not use with potassium penicillin or potassium bromide.

#### Drug Interactions

No drug interactions are reported in animals.

### Instructions for Use

One gram of potassium citrate provides 9.26 mEq of potassium. Administer with meals.

### Patient Monitoring and Laboratory Tests

Monitor serum potassium levels. Normal potassium is 4-5.5 mEq/L (dogs) and 4.3-6.0 mEq/L (cats). Monitor ECG in patients that may be prone to arrhythmias.

### Formulations

- Potassium citrate is available in 5-mEq and 10-mEq tablets. Some formulations are in combination with potassium chloride. Potassium citrate tablets in a delayed-released tablet are also available.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 2.2 mEq/100 kcal of energy/day PO or 0.5 mEq/kg per day PO. Higher doses have been used safely in some animals. (1000 mg potassium citrate = 9.26 mEq potassium.)

### Large Animal Dosage

No doses have been reported for large animals.

### Regulatory Information

No withdrawal times necessary.

## Potassium Gluconate

**Trade and other names:** Kaon, Tumil-K, and generic brands

**Functional classification:** Potassium supplement

### Pharmacology and Mechanism of Action

Potassium supplement. Used for treatment of hypokalemia. Potassium gluconate exists in an anhydrous form and a monohydrate form. Six grams of potassium gluconate anhydrous are equivalent to 1 g potassium; 6.45 g potassium gluconate monohydrate are equivalent to 1 g potassium. One gram potassium gluconate is equal to 4.27 mEq of potassium. Other potassium supplements include potassium chloride, potassium acetate, potassium bicarbonate, and potassium citrate.

## Indications and Clinical Uses

Potassium gluconate is used for the treatment of hypokalemia and renal tubular acidosis. Potassium supplements are indicated for treating hypokalemia. Hypokalemia may occur with some diseases or as a consequence of diuretic use. In most patients, potassium chloride is the supplement of choice for hypokalemia.

### Precautionary Information

#### Adverse Reactions and Side Effects

Toxicity from high potassium concentrations can be dangerous. Hyperkalemia can lead to cardiovascular toxicity (bradycardia and arrest) and muscular weakness. Oral potassium supplements can cause nausea and stomach irritation.

#### Contraindications and Precautions

Use cautiously in animals with kidney disease.

#### Drug Interactions

No drug interactions are reported in animals.

## Instructions for Use

One gram of potassium gluconate provides 4.27 mEq of potassium.

## Patient Monitoring and Laboratory Tests

Monitor serum potassium levels. Normal potassium is 4-5.5 mEq/L (dogs) and 4.3-6.0 mEq/L (cats). Monitor ECG in patients that may be prone to arrhythmias.

## Formulations

- Potassium gluconate is available in a 2-mEq tablet (equivalent to 500 mg potassium gluconate).
- Kaon elixir is a 20-mEq potassium/15 mL elixir (containing 4.68 grams potassium gluconate).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Potassium gluconate is soluble in water.

## Small Animal Dosage

### Dogs

- 0.5 mEq/kg q12-24h PO.

### Cats

- 2-8 mEq/day divided twice daily PO.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

No withdrawal times are necessary.

## Potassium Iodide

**Trade and other names:** Quadrial

**Functional classification:** Antifungal, expectorant

## Pharmacology and Mechanism of Action

Potassium iodide is used as an iodide supplement. It also has some antimicrobial properties, although the exact mechanism is uncertain. The antimicrobial activity has

been used as an adjunctive treatment for zygomycosis, conidiobolomycosis, and fungal granuloma. Iodide is also important for thyroid gland function and has been used to treat some thyroid disorders. Potassium iodide also may irritate the respiratory tract and has been used as an expectorant.

### **Indications and Clinical Uses**

Potassium iodide has been used to treat fungal granulomatous disease and infections associated with zygomycetes. In small animals, it has been used for sporotrichosis. The antifungal treatment has been questioned for animals because the efficacy is not established. Because it may increase respiratory secretions, it has been used as an expectorant, but the efficacy has not been established. In people, iodide has been used to treat hyperthyroidism, but effectiveness for this use in cats has not been established. Potassium iodide is also used to protect the thyroid gland from radiation injury in the event of a radiation emergency (accidental exposure to radiation) or following administration of radioactive iodide.

Ethylenediamine dihydroiodide (EDDI) is another source of iodide that is used as a nutritional source of iodine in cattle. Sodium iodide also is used, particularly in large animals. See sodium iodide and iodide monographs for more information.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

High doses can produce signs of iodism, which include lacrimation, irritation of mucous membranes, swelling of eyelids, cough, dry scruffy coat, and hair loss. Potassium iodide has a bitter taste and can cause nausea and salivation. Potassium iodide administration has been associated with cardiomyopathy in cats. Its use may cause abortion in horses or limb deformities in foals.

#### **Contraindications and Precautions**

Do not administer to foals or pregnant animals (abortion is possible). Do not administer intravenously.

#### **Drug Interactions**

No known drug interactions.

### **Instructions for Use**

Clinical use in animals is primarily empirical. The doses and indications listed have not been tested in clinical trials. Other, more proven drugs for these indications should be considered as alternatives.

### **Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

### **Formulations**

Iodide has been administered as a 1-g/mL potassium iodine saturated solution (SSKI) or as a 65-mg/mL solution. It also has been administered as a 10% potassium iodide/5% iodine solution given orally with food. The saturated solution (1 g/mL) yields 38 mg per drop. A 10% solution of potassium iodide (10%) yields 6.3 mg of iodine per drop. It is also available in tablets of 145 mg of iodine.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze solutions. Inorganic potassium iodide is unstable in light, heat, and excess humidity.

## Small Animal Dosage

### Dogs and Cats

- Fungal infections: start with 5 mg/kg q8h PO and increase gradually to 25 mg/kg q8h PO.
- Emergency treatment after radiation exposure: 2 mg/kg PO per day.
- Expectorant: 5 mg/kg q8h PO.

## Large Animal Dosage

### Cattle

- 10-15 g/day (adult cattle) PO for 30-60 days.
- 5-10 g/day (calves) PO for 30-60 days.
- Feed supplement and other indications: (see iodide monograph for EDDI doses and sodium iodide monograph for other doses).

### Horses

- 10-40 mg/kg per day (using inorganic potassium iodide).
- 10-15 g/day (adult horse) PO for 30-60 days.
- 5-10 g/day (pony) PO for 30-60 days.
- See iodide monograph for EDDI doses and sodium iodide monograph for other doses.

## Regulatory Information

No regulatory information is available. Because of low risk of residues, no withdrawal times are suggested.

## Potassium Phosphate

**Trade and other names:** K-Phos, Neutra-Phos-K, and generic brands

**Functional classification:** Phosphate supplement

## Pharmacology and Mechanism of Action

Phosphorous supplement. Potassium phosphate is used for severe hypophosphatemia associated with diabetic ketoacidosis. It also acidifies the urine.

## Indications and Clinical Uses

Potassium phosphate has been used to reduce calcium urinary secretion in patients prone to calcium urinary calculi and to promote a more acid urine. This drug should not be used to supplement potassium. In most patients, potassium chloride is the supplement of choice for hypokalemia.

## Precautionary Information

### Adverse Reactions and Side Effects

Intravenous administration can cause hypocalcemia.

### Contraindications and Precautions

Use cautiously in animals with renal disease.

### Drug Interactions

No drug interactions are reported in animals.

**Instructions for Use**

Potassium phosphate use in animals is primarily as a urinary acidifier or treatment of hypophosphatemia.

**Patient Monitoring and Laboratory Tests**

Monitor calcium, potassium, and phosphorus levels in treated animals.

**Formulations**

- Potassium phosphate is currently not available in tablets (previously 500 mg containing 114 mg [3.7 mmol] phosphorus). Oral solutions can be made from powdered concentrate mixed with water for oral administration.
- It is also available in 224 mg of monobasic potassium phosphate and 236 mg of dibasic potassium phosphate (3 mmol [93 mg] of phosphorus) per mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats**

- 0.03-0.12 mmol/kg/hr IV for acute treatment.
- 0.1 mmol/kg/day IV for daily supplementation.
- 4 mg/kg phosphorus (approximately 0.1 mmol/kg) PO up to 4 times daily.

**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

No withdrawal times are necessary.

**Pradofloxacin**

Pray doe-floks'ah-sin

**Trade and other names:** Veraflox

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Fluoroquinolone antibacterial drug. Pradofloxacin is of the new generation (third generation) of fluoroquinolones. This new generation of fluoroquinolones, with substitutions at the C-8 position, have as their advantage a broader spectrum that includes anaerobic bacteria and gram-positive cocci. The difference in spectrum of activity is largely caused by increased activity against the DNA gyrase of gram-positive bacteria, rather than activity against topoisomerase IV, which is the target in gram-positive bacteria for the older quinolones (e.g., enrofloxacin, ciprofloxacin, marbofloxacin, and orbifloxacin). These newer fluoroquinolones also include the human drugs gatifloxacin, gemifloxacin, and moxifloxacin. Susceptibility data indicate that pradofloxacin is more active than other fluoroquinolones against bacterial isolates from dogs and cats, including *Escherichia coli*, *Staphylococcus*, and anaerobes. Pradofloxacin is approved for use in cats in the US, but for both dogs and cats in Europe and Canada.

Pradofloxacin is almost 100% absorbed in dogs and has an elimination half-life of approximately 7 hours. The oral absorption of the tablet in cats is 70%, but is lower

with the oral suspension. The half-life in cats is approximately 7-9 hours. In cats and dogs, plasma protein binding is 30% and 35%, respectively.

### Indications and Clinical Uses

Pradofloxacin has been evaluated in dogs and cats, with efficacy studies published in research abstracts and clinical reports in which it has been used for treating skin and soft tissue infections in dogs and cats, oral infections (periodontal therapy), respiratory infections in cats, and UTIs. At a dose of 3 mg/kg orally, it was effective for treatment of UTIs in dogs, and at 3 or 5 mg/kg, it was effective for canine pyoderma. At a dose of 5 mg/kg in a 2.5% oral suspension, it was effective for UTIs in cats. It has been used to effectively treat infections caused by *Chlamydophila felis* or *Mycoplasma* in cats (5 mg/kg q12h PO for 28 days) and was as effective as doxycycline. It has been used to treat feline rhinitis caused by *Mycoplasma*, *Bordetella*, streptococci, or staphylococci at a dose of 5 mg/kg once daily for 7 doses. It has been effective (5 mg/kg per day) for treatment of feline blood infections caused by *Mycoplasma hemofelis*.

### Precautionary Information

#### Adverse Reactions and Side Effects

Safety studies have been completed in cats associated with approval in the US and in dogs and cats in Europe. It has been tolerated well in cats with no adverse effects that are different from other approved fluoroquinolones. Field trials in cats in the US showed that the most common adverse effect was diarrhea or loose stools. In cats, administration at high doses of six times the label dose did not cause ocular problems. In dogs and cats, at high doses pradofloxacin has caused bone marrow suppression, but this has not been reported from clinical use at approved doses.

#### Contraindications and Precautions

No contraindications or precautions are available. Because it is similar to other fluoroquinolones, use cautiously in young dogs that may be susceptible to articular cartilage injury. Risks during pregnancy in dogs and cats are not known, but pradofloxacin induced eye malformations at high doses in rats.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Pradofloxacin may be used for a variety of infections in dogs and cats with similar indications as for other fluoroquinolones, in addition to those listed in the clinical uses sections.

### Patient Monitoring and Laboratory Tests

The CLSI break point for susceptibility is  $\leq 0.25$  mcg/mL for both dogs and cats.

### Formulations

- Formulations contain pradofloxacin in a 2.5% oral suspension in the US and Europe and 15-, 60-, and 120-mg tablets in Europe.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 3-5 mg/kg q24h PO.

#### Cats

- Tablets: 3-5 mg/kg q24h PO.
- Oral suspension: 5-7.5 mg/kg q24h PO.



**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. It should not be used in food-producing animals. Extralabel use of fluoroquinolones in food-producing animals is prohibited.

**Pralidoxime Chloride**

prah-lih-doks'eem klor'ide

**Trade and other names:** 2-PAM and Protopam chloride

**Functional classification:** Antidote

**Pharmacology and Mechanism of Action**

Pralidoxime chloride is an oxime that is used as an adjunct to atropine for treatment of intoxication. Organophosphate intoxication results in inactivation of cholinesterase enzymes and excess accumulation of acetylcholine. Pralidoxime (also known as 2-PAM) is used to reactivate acetylcholinesterase by promoting dephosphorylation. Pralidoxime is well absorbed from IM administration, but it does not cross the blood–brain barrier. After absorption, the half-life is short, necessitating repeated administrations.

**Indications and Clinical Uses**

Pralidoxime chloride is used for treatment of organophosphate toxicosis. Administer promptly after organophosphate intoxication is identified. It also has been used to treat overdoses of other anticholinesterase drugs such as neostigmine, pyridostigmine, and edrophonium.

**Precautionary Information****Adverse Reactions and Side Effects**

Intramuscular injections cause pain. Rapid IV injections may bind calcium and cause muscle spasms. Rapid injections also may cause heart and respiratory problems. Use during pregnancy may produce teratogenic effects.

**Contraindications and Precautions**

Pralidoxime treatment should not be used for carbamate intoxication. Do not administer rapidly intravenously or it may cause respiratory depression and other problems.

**Drug Interactions**

No drug interactions have been reported. However, other drugs should be avoided when treating organophosphate poisoning. These drugs include aminoglycosides, barbiturates, phenothiazine tranquilizers (acepromazine), and neuromuscular blocking agents.

**Instructions for Use**

Dilute formulation in glucose solution before IV administration. Give slowly IV. Administer atropine (0.1 mg/kg) when using pralidoxime. Recovery from organophosphate poisoning may take 48 hours. When treating intoxication, consult a poison control center for precise guidelines.

### Patient Monitoring and Laboratory Tests

Monitor for signs of organophosphate poisoning to determine if repeated doses are necessary. Monitor heart rate and rhythm and respiratory rate. It may be possible to monitor cholinesterase activity from a blood sample to confirm organophosphate poisoning (consult local diagnostic laboratory).

### Formulations

- Pralidoxime chloride is available in a 1-g vial to be reconstituted in 20 mL of water (50-mg/mL injection). pH of solution is 3.5-4.5.

### Stability and Storage

Store powder at room temperature and protect from light. Reconstituted solution should be stored below 25° C and protected from light. Discard reconstituted solution after 3 hours.

### Small Animal Dosage

- 20 mg/kg up to 50 mg/kg q8-12h IM or IV (initial dose slow). Dilute solution in glucose and infuse slowly IV.

### Large Animal Dosage

#### Cattle, Sheep, and Pigs

- 20-50 mg/kg q8h (administered as a 10% solution) IM or via slow IV infusion, or as needed. Frequency can be assessed by monitoring clinical signs.

### Regulatory Information

Cattle and pig withdrawal times (extralabel): 6 days for milk and 28 days for meat.

## Praziquantel

pray-zih-kwon'tel

**Trade and other names:** Droncit and Drontal (combination with febantel)

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Antiparasitic drug. Action on parasites related to neuromuscular toxicity and paralysis via altered permeability to calcium.

### Indications and Clinical Uses

Praziquantel is widely used to treat intestinal infections caused by cestodes (*Dipylidium caninum*, *Taenia pisiformis*, and *Echinococcus granulosus*) and removal and control of canine cestode *Echinococcus multilocularis*. In cats, it is used for removal of feline cestodes *D. caninum* and *T. taeniaeformis*. In horses, it is used to treat tapeworms (*Anoplocephala perfoliata*).

### Precautionary Information

#### Adverse Reactions and Side Effects

Vomiting occurs at high doses. Anorexia and transient diarrhea have been reported. It is safe in pregnant animals and during lactation.

**Contraindications and Precautions**

Avoid use in cats younger than 6 weeks and dogs younger than 4 weeks. Praziquantel has been safe in pregnancy.

**Drug Interactions**

No drug interactions have been reported in animals.

**Instructions for Use**

Praziquantel is one of the most common drugs used for tapeworm treatment. It has a wide margin of safety. Some formulations of praziquantel are available in combination (e.g., combination of praziquantel and febantel, combination of ivermectin and praziquantel, moxidectin, and praziquantel).

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Praziquantel is available in 23- and 34-mg tablets and 56.8-mg/mL injection. It is available as 13.6 mg praziquantel and 54.3 mg pyrantel, or 18.2 mg praziquantel and 72.6 mg pyrantel, or 27.2 mg praziquantel and 108.6 mg pyrantel. It is also available in pastes and gels, and they are available in pastes and gels for horses in combination with other drugs (e.g., ivermectin, moxidectin, febantel).

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs**

- Dogs <6.8 kg: 7.5 mg/kg once PO.
- Dogs >6.8 kg: 5 mg/kg once PO.
- Dogs <2.3 kg, 7.5 mg/kg once IM or SQ.
- Dogs 2.7-4.5 kg: 6.3 mg/kg once IM or SQ.
- Dogs >5 kg: 5 mg/kg once IM or SQ.
- Paragonimus in dogs (lung worms): 23 mg/kg PO q8h for 3 days.

**Cats (all doses given once)**

- <1.8 kg: 11.4 mg/cat PO.
- 1.8 kg to 2.2 kg: 11.4 mg/cat SQ or IM.
- 2.3 kg to 4.5 kg: 22.7 mg/cat SQ or IM.
- 2.3 kg to 5 kg: 23 mg/cat PO.
- >5 kg: 34.5 mg/cat, PO, or 34.1 mg/cat, SQ or IM.

**Large Animal Dosage****Horses**

- 1.5-2.5 mg/kg PO.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Prazosin

pray'zoe-sin

**Trade and other names:** Minipress

**Functional classification:** Vasodilator

### Pharmacology and Mechanism of Action

Alpha<sub>1</sub>-adrenergic blocker. Prazosin is a vasodilator that is a selective blocker for the alpha<sub>1</sub>-adrenergic receptor, but it is not selective for either alpha<sub>1a</sub> or alpha<sub>1b</sub>. Its action is similar to phenoxybenzamine, but it produces less tachycardia than nonselective alpha-antagonist drugs. Prazosin decreases tension in both arterial and venous vascular smooth muscle. It relaxes smooth muscle, especially of vasculature. Prazosin is used as a vasodilator and to relax smooth muscle (occasionally urethral muscle). The alpha<sub>1b</sub> adrenoreceptors regulate vascular tone, and the alpha<sub>1a</sub> adrenoreceptors regulate urethral smooth muscle tone. For specific urinary smooth muscle relaxation, the drugs tamsulosin (Flomax) and silodosin (Rapaflo) are more specific for the alpha<sub>1a</sub> receptor.

### Indications and Clinical Uses

Prazosin has been used in people for vasodilation and the management of hypertension that is not responsive to other drugs. Prazosin has been used to a limited extent in veterinary medicine to produce balanced vasodilation. There are no controlled studies to establish efficacy and dose, and indications are derived from anecdotal use and extrapolation from human medicine. It has been used in cats with urethral obstruction to improve urine flow. There is limited experience, but some evidence, that in comparison to phenoxybenzamine, it produced fewer recurrence rates of urethral obstruction (0.5 mg per cat every 8 hours, PO). It has also been used experimentally in horses to improve digital perfusion in the treatment of laminitis. Long-term administration is not common because tolerance may develop with chronic use.

### Precautionary Information

#### Adverse Reactions and Side Effects

High doses cause vasodilation and hypotension.

#### Contraindications and Precautions

Use cautiously in animals with compromised cardiac function. It may lower blood pressure and decrease cardiac output.

#### Drug Interactions

No drug interactions have been reported in animals, but combined with other vasodilators may produce severe lowering of blood pressure.

### Instructions for Use

Titrate dose to needs of individual patient. Results of clinical studies in animals have not been reported; therefore use in animals (and doses) is based on experience in people or anecdotal experience in animals.

### Patient Monitoring and Laboratory Tests

Monitor for hypotension and reflex tachycardia.

### Formulations

Prazosin is available in 1-, 2-, and 5-mg capsules.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats**

- 0.5-2 mg per dog, or 0.25-1 mg per cat (0.07 mg/kg, or approximately 1 mg per 15 kg) q8-12h PO.
- Cats with urethral obstruction: 0.5 mg per cat PO q8h.

**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

**Prednisolone Sodium Succinate**

pred-niss-oh'lonē soe'dee-um suk'sih-nate

**Trade and other names:** Solu-Delta-Cortef

**Functional classification:** Corticosteroid

**Pharmacology and Mechanism of Action**

Prednisolone sodium succinate is the same as prednisolone, except that this is a water-soluble formulation intended for acute therapy when high IV doses are needed for rapid effect.

**Indications and Clinical Uses**

Prednisolone sodium succinate has similar uses as prednisolone in other forms, except this is used when prompt response is needed from injection, especially at high doses. Methylprednisolone sodium succinate (Solu-Medrol) has also been used for similar indications. Uses include treatment of immune-mediated diseases (e.g., pemphigus and hemolytic anemia), spinal cord trauma, and adrenocortical insufficiency. Large animal uses include treatment of inflammatory conditions and treatment of recurrent airway obstruction (RAO) in horses. In cattle, corticosteroids have been used in the treatment of ketosis. The use of prednisolone for treatment of shock, snakebites, and head trauma is discouraged because of lack of proven efficacy or high risk of adverse effects.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are not expected from single administration. However, with repeated use, other side effects are possible. Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic-pituitary-adrenal (HPA) axis suppression. Adverse effects include gastrointestinal ulceration, diarrhea, steroid hepatopathy, diabetes mellitus, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, impaired wound healing, and immunosuppression. In cats, polyuria is less common than in dogs, and it has not increased calcium excretion or calcium-containing calculi. With high doses of prednisolone

sodium succinate, there is a risk of gastrointestinal bleeding. In horses, in addition to the previously listed adverse effects, there may be an increased risk of laminitis, although documentation of this effect has been controversial.

### **Contraindications and Precautions**

Use cautiously in patients with a risk of gastrointestinal ulcers and bleeding or infection or in animals in which growing or healing is necessary. Use prednisolone sodium succinate cautiously in patients with kidney disease because it may cause azotemia. Use cautiously in pregnant animals because fetal abnormalities have been reported in laboratory rodents.

### **Drug Interactions**

Administration of corticosteroids with NSAIDs will increase the risk of gastrointestinal injury. Do not mix prednisolone sodium succinate with solutions containing calcium.

## **Instructions for Use**

Doses for prednisolone are based on severity of underlying condition. Use of prednisolone sodium succinate is often at high doses for acute treatment.

## **Patient Monitoring and Laboratory Tests**

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an ACTH stimulation test to monitor adrenal function. Corticosteroids can increase liver enzymes—especially alkaline phosphatase—without inducing liver pathology. Prednisolone can increase white blood cell count and decrease lymphocyte count. It can increase serum albumin, glucose, triglycerides, and cholesterol. Corticosteroid administration may decrease conversion of thyroid hormones to its active form. Prednisolone and prednisone at high doses for several weeks may produce significant proteinuria and glomerular changes in some dogs.

## **Formulations**

- Prednisolone sodium succinate is available in 100- and 500-mg vials for injection (10, 20, and 50 mg/mL). For some indications, methylprednisolone sodium succinate (Solu-Medrol) has been substituted.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Prednisolone sodium succinate should be used immediately after reconstitution. Do not freeze. If solution becomes cloudy, do not administer intravenously.

## **Small Animal Dosage**

### **Dogs and Cats**

- Shock (effectiveness of this use is controversial): 15-30 mg/kg IV (repeat in 4-6 hours).
- CNS trauma: 15-30 mg/kg IV, taper to 1-2 mg/kg q12h.
- Anti-inflammatory: 1 mg/kg/day IV.
- Replacement therapy: 0.25-0.5 mg/kg/day IV.
- Intermittent treatment (pulse therapy) of pemphigus foliaceus: 10 mg/kg IV.

## **Large Animal Dosage**

### **Horses**

- 0.5-1 mg/kg q12-24h IM or IV. Intravenous dose should be given slowly over 30-60 seconds.

- Treatment of shock: Although efficacy for treating shock has not been established, recommended doses are 15-30 mg/kg IV; repeat dose in 4-6 hours.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use with withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 4

## Prednisolone, Prednisolone Acetate

**Trade and other names:** Delta-Cortef, PrednisTab, and generic brands

**Functional classification:** Corticosteroid

### Pharmacology and Mechanism of Action

Glucocorticoid anti-inflammatory drug. Anti-inflammatory effects are complex, but via binding to cellular glucocorticoid receptors, prednisolone acts to inhibit inflammatory cells and suppresses expression of inflammatory mediators. Prednisolone is approximately four times more potent than cortisol but only one seventh as potent as dexamethasone. Prednisolone is available as the base (usually as a tablet) or as an injectable acetate form, which can be administered intramuscularly or intraarticularly.

### Indications and Clinical Uses

Prednisolone, like other corticosteroids, is used to treat a variety of inflammatory and immune-mediated disease. The accompanying dosing section lists a range of doses for replacement therapy, anti-inflammatory therapy, and immunosuppressive therapy. Large animal uses include treatment of inflammatory conditions, especially musculoskeletal disorders. In horses, prednisolone has been used for treatment of RAO, formerly called chronic obstructive pulmonary disease (COPD). In cattle, corticosteroids have been used in the treatment of ketosis. The prednisolone and trimeprazine formulation (Temaril-P) has been effective for treating pruritus in dogs. (See trimeprazine for further details.)

### Precautionary Information

#### Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, behavior changes, and HPA axis suppression. Adverse effects include gastrointestinal ulceration, steroid hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, increased risk of diabetes, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs. In horses, in addition to the previously listed adverse effects, there may be an increased risk of laminitis, although documentation of this effect has been controversial.

#### Contraindications and Precautions

Use cautiously in patients with a risk of gastrointestinal ulcers and bleeding or infection or in animals in which growing or healing is necessary. Use prednisolone cautiously in patients with kidney disease because it may cause azotemia. Use prednisolone cautiously in pregnant animals because fetal abnormalities have been reported in laboratory rodents. Do not administer prednisolone acetate intravenously.

In some species—particularly horses and cats—prednisolone (the active form) is preferred for oral treatment rather than prednisone.

### Drug Interactions

Administration of corticosteroids with NSAIDs will increase the risk of gastrointestinal injury. Corticosteroids may inhibit conversion of T<sub>4</sub> thyroid hormone to the active form T<sub>3</sub>.

### Instructions for Use

Doses for prednisolone are of a broad range and based on severity of underlying condition. Doses for long-term treatment may eventually be tapered to 0.5 mg/kg q48h PO.

### Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an ACTH stimulation test to monitor adrenal function. Corticosteroids can increase liver enzymes—especially alkaline phosphatase—without inducing liver pathology. Prednisone can increase white blood cell count and decrease lymphocyte count. It can increase serum albumin, glucose, triglycerides, and cholesterol. Corticosteroid administration may decrease conversion of thyroid hormones to active form. Prednisolone and prednisone at high doses for several weeks may produce significant proteinuria and glomerular changes in some dogs.

### Formulations

- Prednisolone is available in 5- and 20-mg tablets, 3-mg/mL syrup, and 25-mg/mL acetate suspension injection (10 and 50 mg/mL in Canada). Prednisolone is also available in combination with trimeprazine (Temaril-P). (See trimeprazine for more information.) Prednisolone sodium phosphate orally disintegrating tablets (ODT) are available for people. These tablets are available in sizes of 5, 10, 15, and 30 mg.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Prednisolone is slightly soluble in water, but it is more soluble in ethanol. If diluted first in ethanol, it may be compounded into oral liquid formulations with good stability for 90 days. Prednisolone acetate is insoluble in water. Do not freeze.

### Small Animal Dosage

#### Dogs

- Anti-inflammatory: 0.5-1 mg/kg q12-24h IV, IM, or PO initially, then taper to q48h at a dose of 0.3-0.5 mg/kg.
- Immunosuppressive: 2.2-6.6 mg/kg/day IV, IM, or PO initially, then taper to 2-4 mg/kg q48h. Initial doses rarely need to exceed 4 mg/kg per day.
- Neurologic disease (steroid responsive): Start with 2 mg/kg q12h PO for 2 days, followed by gradual tapering to 1 mg/kg, then 0.5 mg/kg, and eventually to 0.5 mg/kg every other day.
- Replacement therapy: 0.2-0.3 mg/kg/day PO.
- Cancer therapy (e.g., COAP protocol): 40 mg/m<sup>2</sup> q24h for 7 days, then 20 mg/m<sup>2</sup> every other day PO.



## 670 Prednisone

### Cats

- Same as for dogs, except that for many conditions they require twice the dog dose.

### Large Animal Dosage

#### Horses

- Prednisolone acetate suspension: 100-200 mg total dosage IM.
- Prednisolone tablets: 0.5-1 mg/kg q12-24h PO. Taper to lower dose for long-term treatment.

#### Cattle

- Treatment of ketosis: 100-200 mg total dosage IM.

### Regulatory Information

Cattle withdrawal times for prednisolone acetate: 5 days for meat, 72 hours for milk (in Canada).

Withdrawal times are not established for animals that produce food in the US.

For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Prednisone

pred'nih-sone

**Trade and other names:** Deltasone, Meticorten, and generic brands

**Functional classification:** Corticosteroid

### Pharmacology and Mechanism of Action

Glucocorticoid anti-inflammatory drug. The effect of prednisone is attributed to prednisolone. After administration, prednisone is converted to prednisolone. Anti-inflammatory effects are complex, but via binding to cellular glucocorticoid receptors, prednisolone acts to inhibit inflammatory cells and suppresses expression of inflammatory mediators. Prednisolone is approximately four times more potent than cortisol but only one seventh as potent as dexamethasone. Prednisone appears to be well absorbed and converted to active drug in dogs. However, in horses and cats, administration of prednisone results in low systemic levels of the active drug prednisolone, either because of poor absorption of prednisone or because of a deficiency in converting prednisone into prednisolone.

### Indications and Clinical Uses

Prednisone, like other corticosteroids, is used to treat a variety of inflammatory and immune-mediated diseases. In cats, prednisone may produce therapeutic failures, and prednisolone (active drug) is preferred. There is evidence of poor conversion of prednisone to prednisolone or poor absorption of prednisone in cats, and prednisolone or another active drug (e.g., triamcinolone) should be used instead. There are several large animal doses cited (similar to prednisolone); however, because of poor activity in horses, the use is discouraged.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, behavior changes, and HPA axis suppression. Adverse effects include gastrointestinal ulceration, diarrhea hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, delayed wound healing, and immunosuppression. Secondary infections can occur as a result of immunosuppression and include demodicosis, toxoplasmosis, fungal infections, and UTIs.

### Contraindications and Precautions

Use cautiously in patients with a risk of gastrointestinal ulcers and bleeding or infection or in animals in which growing or healing is necessary. Use prednisone cautiously in patients with renal disease because it may cause azotemia. Use prednisone cautiously in pregnant animals because fetal abnormalities have been reported in laboratory rodents.

### Drug Interactions

Administration of corticosteroids with NSAIDs will increase the risk of gastrointestinal injury.

## Instructions for Use

Prednisolone and prednisone can be used interchangeably in dogs. However, cats and horses may have problems converting prednisone to the active prednisolone or problems with oral absorption of prednisone, and prednisolone should be used instead. (Alternatively, methylprednisolone or triamcinolone can be used in cats.) As for prednisolone, the doses vary across a broad range, based on severity of the underlying condition. Consult the dosing section for the range of doses administered for each condition.

## Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an ACTH stimulation test to monitor adrenal function. Corticosteroids can increase liver enzymes—especially alkaline phosphatase—without inducing liver pathology. Corticosteroid administration may decrease conversion of thyroid hormones to active form. However, in dogs receiving anti-inflammatory doses of prednisone, total  $T_4$  concentrations may be decreased but not free  $T_4$  ( $fT_4$ ).

## Formulations

- Prednisone is available in 1-, 2.5-, 5-, 10-, 20-, 25-, and 50-mg tablets; 1-mg/mL syrup (Liquid Pred in 5% alcohol); 1-mg/mL oral solution (in 5% alcohol); and 10- and 40-mg/mL prednisone suspension for injection (Meticorten; availability has been limited).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Prednisone is slightly soluble in water, and it is soluble in ethanol. Prednisone has been prepared by first dissolving in ethanol, then mixing with syrups and flavorings. No loss occurred, but crystallization is common in aqueous vehicles. Prednisone tablets have been crushed and mixed with syrups and other flavorings, stored for 60 days, and found to produce equal bioavailability as tablets in people.

## Small Animal Dosage

### Dogs

- Anti-inflammatory: 0.5-1 mg/kg q12-24h IV, IM, or PO initially, then taper to q48h at a dose of 0.3-0.5 mg/kg.
- Immunosuppressive: 2.2-6.6 mg/kg/day IV, IM, or PO initially, then taper to 2-4 mg/kg q48h. Initial doses rarely need to exceed 4 mg/kg per day.
- Replacement therapy: 0.2-0.3 mg/kg/day PO.
- Neurologic disease (steroid responsive): Start with 2 mg/kg q12h PO for 2 days, followed by gradual tapering to 1 mg/kg, then 0.5 mg/kg, and eventually to 0.5 mg/kg every other day.
- Cancer therapy (e.g., COAP protocol): 40 mg/m<sup>2</sup> q24h for 7 days, then 20 mg/m<sup>2</sup> every other day PO.

### Cats

- Not recommended for cats because of inability to form active metabolite. However, if use is attempted, higher doses than used in dogs will be needed.

## Large Animal Dosage

### Horses

- Prednisone suspension (Meticorten) (label dose): 100-400 mg per horse (0.22-0.88 mg/kg) as a single dose IM to be repeated every 3-4 days. No oral doses are listed for horses because of inability of oral treatment to produce active prednisolone concentrations.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 4

## Pregabalin

Pree ga'bah-lin

**Trade and other names:** Lyrica

**Functional classification:** Analgesic, Anticonvulsant

## Pharmacology and Mechanism of Action

Analgesic and anticonvulsant. Pregabalin is similar in action to gabapentin, which is an analogue of the inhibitory neurotransmitter GABA. However, like gabapentin, it is not an agonist or antagonist for the GABA receptor. The anticonvulsant effect occurs via inhibition of calcium channels in neurons. Pregabalin inhibits the alpha-2-delta ( $\alpha_2\delta$ ) subunit of the N-type voltage-dependent calcium channel on neurons. Via inhibition, it reduces calcium influx that is needed for release of neurotransmitters—specifically excitatory amino acids—from presynaptic neurons. Blocking the channels has little effect on normal neurons but may suppress simulated neurons involved in seizure activity and some forms of pain. In humans, pregabalin has better oral absorption and a longer half-life than gabapentin. Pregabalin relies on renal excretion, probably to a greater extent than gabapentin.

Pregabalin half-life in dogs is approximately 7 hours, compared with 3-4 hours for gabapentin, and it remained above the estimated effective levels for 11 hours after

dosing. Oral absorption in dogs was 98%. In cats, after 4 mg/kg oral, plasma concentrations were above the levels estimated to be effective for over 12 hours, with a half-life of 10 hours. In horses, it has low oral absorption (16%) with a half-life of 8 hours and, at a dose of 4 mg/kg oral, it produces plasma concentrations in the same therapeutic range as for people.

### Indications and Clinical Uses

In people, pregabalin is popular for treating neuropathic pain syndromes associated with diabetes, postherpetic neuralgia, and fibromyalgia. Pregabalin is also used as an anticonvulsant. As an analgesic in animals, it has been used to treat neuropathic pain that does not respond to NSAIDs or opiates. It may be combined with those agents. When used to treat epilepsy, pregabalin has reduced seizure frequency in refractory patients when combined with phenobarbital and potassium bromide. Therefore it is considered when the seizures have become refractory to other drugs in conjunction with other anticonvulsants. For treating pain, regimens have been mostly derived from anecdotal evidence or extrapolation from human medicine.

In horses, it can produce concentrations in the therapeutic range for people, but safety and effectiveness have not been studied.

### Precautionary Information

#### Adverse Reactions and Side Effects

Sedation and ataxia are reported adverse effects that can occur at doses as high as 3-4 mg/kg. As dose increases in dogs, sedation is more likely. In people, a withdrawal syndrome from abrupt discontinuation has been described, but it is not reported in animals.

#### Contraindications and Precautions

No known contraindications. Pregabalin, like gabapentin, is excreted in the urine, and liver disease or drug metabolism interactions are not expected to affect the pharmacokinetics. Protein binding is low. In people, it has been used with other anticonvulsants and anesthetics without producing a pharmacokinetic drug interaction.

#### Drug Interactions

There are no reported drug interactions that affect the pharmacokinetics of pregabalin.

### Instructions for Use

Pregabalin may be administered with or without food. Pregabalin has been used in some animals with other drugs such as phenobarbital and bromide. It also has been used to treat neuropathic pain syndromes and can be used with NSAIDs and opioids.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. Routine measurement of plasma concentrations is not widely available, but therapeutic concentrations in people (2.8-8.2 mcg/mL) have been used as a guideline. In some dogs, mild increases in liver enzymes may be observed during treatment.

### Formulations

- Pregabalin is available in 25-, 50-, 75-, 100-, 150-, 200-, 225-, and 300-mg capsules and oral solution of 20 mg/mL.

### Stability and Storage

Store in a tightly sealed container, protected from light and humidity. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- Anticonvulsant dose: 2 mg/kg q8h PO. Start with a low dose and gradually increase to the maximum tolerated dose of 3-4 mg/kg PO.
- Neuropathic pain: Start with 4 mg/kg q12h PO and increase dose gradually if necessary.

### Cats

- Anticonvulsant dose or neuropathic pain dose: start with 2 mg/kg q12h PO and increase to 4 mg/kg q12h PO.

## Large Animal Dosage

### Horses

- 4 mg/kg PO q8h.

## Regulatory Information

Pregabalin is a Schedule V controlled substance. No withdrawal times are available for food animals. For extralabel use with withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Primidone

prih'mih-done

**Trade and other names:** Mylepsin, Neurosyn, and Mysoline (in Canada)

**Functional classification:** Anticonvulsant

## Pharmacology and Mechanism of Action

Anticonvulsant. Primidone is converted to phenylethylmalonamide (PEMA) and phenobarbital, both of which have anticonvulsant activity, but most of the activity (85%) is probably because of the phenobarbital. Phenobarbital acts to potentiate the inhibitory effects of GABA-mediated chloride channels. See the section in this book on [phenobarbital](#) for more information on pharmacology.

## Indications and Clinical Uses

Primidone is used for treating seizure disorders in animals, including epilepsy. The effects of primidone are primarily produced by the presence of the active metabolite, phenobarbital. Although it is possible that some patients with epilepsy that are refractory to phenobarbital alone will respond better to primidone, the number of such cases is low. Primidone is approved for use in dogs, but its use has declined in favor of administration of phenobarbital, bromide, or other anticonvulsants.

## Precautionary Information

### Adverse Reactions and Side Effects

Because primidone is converted to phenobarbital, adverse effects are the same as for phenobarbital. Primidone has been associated with idiosyncratic hepatotoxicity in dogs. Although some labels caution its use in cats, one study in experimental cats determined that it is safe if used at recommended doses.

### Contraindications and Precautions

There may be a higher risk of hepatic toxicity with primidone compared with other anticonvulsants. Primidone should be avoided in animals with liver disease.

### Drug Interactions

Primidone is converted to phenobarbital, which is one of the most potent drugs for inducing hepatic microsomal metabolizing enzymes. Therefore many drugs administered concurrently will have lower (and perhaps subtherapeutic) concentrations because of more rapid clearance. Drugs affected may include theophylline, digoxin, corticosteroids, anesthetics, and other drugs that are substrated for Cytochrome P450 enzymes.

### Instructions for Use

Recommendations are similar to those for phenobarbital. When monitoring therapy with primidone, phenobarbital plasma concentrations should be measured to estimate anticonvulsant effect. When converting a patient from primidone therapy to phenobarbital, the conversion is as follows: 60 mg phenobarbital is approximately 250 mg of primidone.

### Patient Monitoring and Laboratory Tests

Doses should be carefully adjusted via monitoring serum/plasma phenobarbital concentrations. Collect a sample at any time during the dose interval because the timing of the sample is not critical. Avoid the use of plasma separation devices if the tube is to be stored. The therapeutic range in dogs is considered 15-40 mcg/mL (65-180 mmol/L). The optimum range in cats for therapeutic effect is 23-28 mcg/mL. Monitor liver function with bile acid determinations.

### Formulations

- Primidone is available in 50- and 250-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 8-10 mg/kg q8-12h as initial dose PO, then adjust via monitoring to 10-15 mg/kg q8h.

### Large Animal Dosage

- No doses have been reported for large animals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 3

## Procainamide Hydrochloride

proe-kane-ah'mide hye-droe-klor'ide

**Trade and other names:** Pronestyl and generic brands

**Functional classification:** Antiarrhythmic

### Pharmacology and Mechanism of Action

Class I antiarrhythmic drug. Like other Class I antiarrhythmic drugs (similar to quinidine), procainamide will inhibit sodium influx into the cardiac cell via sodium

channel blockade. It will suppress cardiac automaticity and reentrant arrhythmias, primarily in the ventricle. Procainamide is metabolized in people to n-acetyl procainamide (NAPA), which produces other antiarrhythmic actions (Class III drug: potassium channel-blocking effects). However, dogs do not form this metabolite because of an inability to acetylate some drugs.

### **Indications and Clinical Uses**

Procainamide is used in small animals to suppress ventricular ectopic beats and treat ventricular arrhythmias. Studies in experimental dogs with induced arrhythmias have documented efficacy, but clinical use is based primarily on anecdotal experience. It is used primarily during acute treatment and can be administered by injection or tablet. Rarely is long-term treatment used. Procainamide has occasionally been used in horses to suppress ventricular arrhythmias. The availability of commercial forms of procainamide has diminished and the use has declined in favor of other antiarrhythmic agents.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects include cardiac arrhythmias, cardiac depression, tachycardia, and hypotension. In people, procainamide produces hypersensitivity effects (lupuslike reactions), but these have not been reported in animals.

#### **Contraindications and Precautions**

Procainamide can suppress the heart and produce proarrhythmic effects. Use cautiously in animals receiving digoxin because it may potentiate arrhythmias.

#### **Drug Interactions**

Drugs that inhibit cytochrome P450 enzymes (e.g., cimetidine) can potentially increase procainamide concentrations.

### **Instructions for Use**

Because dogs do not produce the active metabolite NAPA, the dose may be higher compared with dosage for people to control some arrhythmias. In animals, there is no evidence that slow-release oral formulations produce longer duration of sustained blood concentrations.

### **Patient Monitoring and Laboratory Tests**

Monitor plasma concentrations during chronic therapy. Effective plasma concentrations in experimental dogs are 20 mcg/mL. However, in some references, concentrations as low as 8-10 mcg/mL are cited to be effective. The metabolite, NAPA, is monitored in people, but dogs do not produce this metabolite. Electrocardiogram should be monitored in treated animals.

### **Formulations**

- Procainamide has been available in 250-, 375-, and 500-mg tablets or capsules and a 100- and 500-mg/mL injection. However, because of diminished use in human medicine in favor of other alternatives, many of the human formulations are no longer available.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Procainamide is soluble in water. When stored, solutions may turn yellow without losing potency. Darker coloration indicates oxidation. Storage of injectable vials in the refrigerator will prevent oxidation. pH of oral compounded products should be 4-6 for maximum stability. Compounded oral products in syrups and flavorings may be stable for 60 days or more, but they should be kept in the refrigerator.

## Small Animal Dosage

### Dogs

- 10-30 mg/kg q6h PO to a maximum dose of 40 mg/kg.
- 8-20 mg/kg IV or IM.
- CRI: Initial loading dose of 10 mg/kg, followed by 20 mcg/kg/min IV CRI; the CRI rate can be increased to 25-50 mcg/kg/min if needed for refractory arrhythmias.

### Cats

- 3-8 mg/kg q6-8h IM or PO.
- CRI: 1-2 mg/kg IV slowly, then 10-20 mcg/kg/min IV.

## Large Animal Dosage

### Horses

- 25-35 mg/kg q8h PO.
- Up to a maximum dose of 20 mcg/kg IV.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Prochlorperazine Edisylate, Prochlorperazine Maleate

proe-klor-pare'ah-zeen ed-iss'ih-late, proe-klor-pare'ah-zeen mal'ee-ate

**Trade and other names:** Compazine

**Functional classification:** Antiemetic, phenothiazine

## Pharmacology and Mechanism of Action

Phenothiazine. Central-acting dopamine ( $D_2$ ) antagonist. Prochlorperazine is related to other phenothiazine antiemetics such as chlorpromazine. Prochlorperazine suppresses dopamine activity in the CNS to produce sedation and prevent vomiting. Antiemetic action also may be related to  $\alpha_2$  and muscarinic blocking effects. There are two salt formulations of prochlorperazine: prochlorperazine edisylate and prochlorperazine maleate. They are therapeutically equivalent. Other phenothiazines include chlorpromazine, perphenazine, promazine, trifluoperazine, and triflupromazine.

## Indications and Clinical Uses

Prochlorperazine is used for sedation, for tranquilization, and as antiemetic. In people, it is also used to treat schizophrenia and nonpsychotic anxiety. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

## Precautionary Information

### Adverse Reactions and Side Effects

Prochlorperazine causes sedation and other side effects attributed to other phenothiazines. It also produces extrapyramidal side effects (involuntary muscle movements) in some individuals. Because of the  $\alpha$ -receptor-blocking properties, it can potentially produce vasodilation and hypotension.



**Contraindications and Precautions**

Like other phenothiazines, it may be contraindicated in some CNS disorders. It may lower seizure threshold in susceptible animals.

**Drug Interactions**

Prochlorperazine may potentiate other sedatives.

**Instructions for Use**

Prochlorperazine is used primarily as an antiemetic in animals. Clinical trials are not available; doses are based primarily on extrapolation and anecdotal experience.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Prochlorperazine is available in 5-, 10-, and 25-mg tablets (prochlorperazine maleate); 1-mg/mL oral solution; and 5-mg/mL injection (prochlorperazine edisylate).

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Prochlorperazine is slightly soluble in water and soluble in ethanol. However, the maleate form is more insoluble in water. Prochlorperazine edisylate may be mixed with fluids such as water for injection. Some yellow discoloration may not affect potency. However, if milky-white precipitate forms in vial, do not use.

**Small Animal Dosage****Dogs and Cats**

- 0.1-0.5 mg/kg q6-8h IM, IV, or SQ.
- 0.15-0.35 mg/kg q6-8h PO.

**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Prochlorperazine Edisylate and Isopropamide Iodide, Prochlorperazine Maleate, and Isopropamide Iodide**

**Trade and other names:** Darbazine

**Functional classification:** Antiemetic, antidiarrheal

**Pharmacology and Mechanism of Action**

Combination product. This combination combines either prochlorperazine edisylate (injectable form) or prochlorperazine maleate (oral form) with isopropamide (isopropamide iodide). Chlorpromazine is a central-acting dopamine antagonist (antiemetic); isopropamide is an anticholinergic drug (atropinelike effects).

## Indications and Clinical Uses

Prochlorperazine is a phenothiazine used to control vomiting; isopropamide is an anticholinergic used to decrease intestinal motility and gastrointestinal secretions. Its use is not common because of decreased availability of formulations and lack of proven efficacy.

### Precautionary Information

#### Adverse Reactions and Side Effects

Side effects are attributed to each component. Prochlorperazine produces phenothiazinelike effects described more fully in the prochlorperazine monograph. Isopropamide may produce effects attributed to excess anticholinergic (antimuscarinic) stimulation and include ileus, urine retention, tachycardia, xerostomia (dry mouth), and behavior changes. Treat overdoses with physostigmine.

#### Contraindications and Precautions

Use of antimuscarinic drugs is contraindicated in animals with gastroparesis and should be used cautiously in animals with diarrhea.

#### Drug Interactions

Isopropamide will interfere with cholinergic drugs or drugs that promote motility (e.g., metoclopramide). Prochlorperazine will potentiate other sedatives.

## Instructions for Use

This combination should be used with caution, especially if considered for repeated doses, in animals with intestinal disease. It can produce ileus.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Prochlorperazine edisylate + isopropamide iodide is available in 3.33-mg prochlorperazine and 1.67-mg isopropamide capsules, and prochlorperazine maleate + isopropamide iodide is available in 4 mg prochlorperazine and 0.28 mg isopropamide per milliliter injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Cats

- 0.14-0.2 mL/kg q12h SQ.

### Dogs

- 0.14-0.2 mL/kg q12h SQ.
- 2-7 kg body weight: 1 capsule q12h PO.
- 7-13 kg body weight: 1-2 capsules q12h PO.

## Large Animal Dosage

No doses have been reported for large animals. The use is discouraged because isopropamide may decrease gastrointestinal motility.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 2

## Promethazine Hydrochloride

proe-meth'ah-zeen hye-droe-klor-ide

**Trade and other names:** Phenergan

**Functional classification:** Antiemetic, phenothiazine

### Pharmacology and Mechanism of Action

Phenothiazine with strong antihistamine effects. Promethazine is used mostly for its antiemetic effects, for which it acts either via the antihistamine receptors or by blocking dopamine receptors associated with vomiting.

### Indications and Clinical Uses

Promethazine is used for treatment of allergy (antihistamine effect) and as an antiemetic (motion sickness). The efficacy for treating allergies in animals has not been established. Other uses in animals have been derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

Promethazine has a risk of producing phenothiazine effects such as sedation and other side effects attributed to other phenothiazines. There also may be anticholinergic effects produced by the antimuscarinic properties in some individuals.

#### Contraindications and Precautions

Promethazine may produce antimuscarinic side effects, but these have not been reported from clinical use in animals.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Results of clinical studies in animals have not been reported. Therefore the use in animals (and doses) is based on experience in people or anecdotal experience in animals.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Promethazine is available in 6.25- and 25-mg/5 mL syrup; 12.5-, 25-, and 50-mg tablets; and 25- and 50-mg/mL injection.

### Stability and Storage

Promethazine hydrochloride is soluble in water. If oxidized, it will turn a blue color and should be discarded. It is sensitive to light and should be protected from light.

### Small Animal Dosage

#### Dogs and Cats

- 0.2-0.4 mg/kg q6-8h IV, IM, PO up to a maximum dose of 1 mg/kg.

### Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).  
RCI Classification: 3

## Propantheline Bromide

proe-pan'theh-leen broe'mide

**Trade and other names:** Pro-Banthine

**Functional classification:** Antidiarrheal

## Pharmacology and Mechanism of Action

Anticholinergic (antimuscarinic) drug. Propantheline blocks acetylcholine receptors to produce parasympatholytic effects (atropinelike effects). It will produce systemic parasympatholytic effects that include decreased gastrointestinal secretions and motility.

## Indications and Clinical Uses

Propantheline is used to decrease smooth muscle contraction and secretion of the gastrointestinal tract. Via the anticholinergic effects, it also has been used to treat vagal-mediated cardiovascular effects, such as bradycardia and heart block. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Because it will produce a profound decrease in gastrointestinal tract motility, its use should be carefully weighed against the potential for adverse effects.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects are attributed to excess anticholinergic (antimuscarinic) effects and include ileus, urine retention, tachycardia, xerostomia (dry mouth), and behavior changes. Treat overdoses with physostigmine.

### Contraindications and Precautions

Do not use in animals with decreased intestinal motility. Use cautiously in animals with heart disease because it may increase heart rate. Do not use in animals with glaucoma.

### Drug Interactions

Propantheline will interfere with cholinergic drugs or drugs that promote motility (e.g., metoclopramide). Bromide concentration in the formulation should be considered for animals also receiving bromide (e.g., potassium bromide) for treatment of epilepsy.

## Instructions for Use

Propantheline has not been evaluated in clinical trials in animals, but propantheline is often the drug of choice for oral therapy in cases where an anticholinergic effect is desired.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Propantheline is available in 7.5- and 15-mg tablets.

## 682 Propiopromazine Hydrochloride

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 0.25-0.5 mg/kg q8-12h PO.

### Large Animal Dosage

- No doses have been reported for large animals. The use is discouraged because of adverse effect on gastrointestinal motility.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Propiopromazine Hydrochloride

proe-pee-oh-prom'ah-zeen hye-droe-klor'idē

**Trade and other names:** Tranvet

**Functional classification:** Antiemetic, phenothiazine

### Pharmacology and Mechanism of Action

Propiopromazine is a phenothiazine with antihistamine effects. It has actions similar to other systemic phenothiazine drugs. Propiopromazine is used mostly for its antiemetic and sedative effects, for which it acts either via the antihistamine receptors or by blocking dopamine receptors. This drug was once registered for human use, but the only formulations currently available are veterinary forms. A related drug is propiomazine.

### Indications and Clinical Uses

Propiopromazine has been used for its antiemetic and sedative effects, for which it acts either via the antihistamine receptors or by blocking dopamine receptors. It also has sedative and tranquilizing effects and has been used in cats and dogs to facilitate handling difficult, excited, or unruly animals. It has also been used as a preanesthetic. The approved label use indicates that it is "intended for administration to dogs as a tranquilizer. It is used as an aid in handling difficult, excited, and unruly dogs, and in controlling excessive kennel barking, car sickness, and severe dermatitis. It is also indicated for use in minor surgery and prior to routine examinations, laboratory procedures, and diagnostic procedures." Despite this labeling, some of these indications are outdated and there are better treatments to manage these conditions.

### Precautionary Information

#### Adverse Reactions and Side Effects

Phenothiazines can cause sedation as a common side effect. Propiopromazine produces extrapyramidal side effects in some individuals.

#### Contraindications and Precautions

It may lower blood pressure via alpha-adrenergic blockade.

#### Drug Interactions

Do not use with other phenothiazines, organophosphates, or procaine.

## Instructions for Use

Results of clinical studies in animals have not been reported, despite indications listed on the product label. Use in animals (and doses) is based on anecdotal experience in animals and the product label.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Propiopromazine has been available as a 20-mg chewable tablet and a 5- or 10-mg/mL injection. Similar human drugs (e.g., propiopromazine) have been discontinued.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- 1.1-4.4 mg/kg q12-24h PO.
- 0.1-1.1 mg/kg IV or IM (range of injectable doses depends on level of sedation needed).

## Large Animal Dosage

- No doses have been reported for large animals. The use is discouraged in horses and ruminants because it may inhibit gastrointestinal motility.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Propofol

proe'poe-fole

**Trade and other names:** Rapinovet, PropoFlo, PropoFlo 28, and PropoFlo Plus (veterinary preparations), and Diprivan (human preparation)

**Functional classification:** Anesthetic

## Pharmacology and Mechanism of Action

Anesthetic. Mechanism of action is not well defined, but it is likely that it produces effects via a similar mechanism as barbiturates. Therefore, it produces depression of the central nervous system (CNS) through its effect on the GABA receptor. Propofol decreases GABA from dissociating from its receptors, thereby increasing chloride conductance through channels, hyperpolarization of post synaptic cell membranes, and inhibition of the postsynaptic neurons. This produces the anesthetic effects observed in animals. Propofol produces a short-acting (10 minutes) anesthesia, followed by a rapid and smooth recovery. The original formulation contained propofol in castor oil and other formulations containing soybean oil, glycerol, and purified egg phosphatide. The newest formulation contains 1% propofol in an emulsion mixture of medium- and long-chain triglycerides that produces greater encapsulation and lower concentration of free propofol.

## Indications and Clinical Uses

Propofol is used as a short-term injectable anesthetic. It may be used as an induction agent followed by inhalation with halothane or isoflurane. The advantage of propofol over other agents is smooth, rapid recovery. It can be used with acepromazine, diazepam,  $\alpha_2$ -agonists (e.g., dexmedetomidine), butorphanol, and inhalant anesthetics. An additional use of propofol is treatment of status epilepticus. It has been used safely and effectively for short-term induction and surgical procedures. It is also appropriate for procedures that require repeated anesthetic episodes in dogs and cats without producing adverse effects.

## Precautionary Information

### Adverse Reactions and Side Effects

Apnea and respiratory depression are the most common adverse effects, which are more likely when the dose is increased. Propofol can induce a dose-dependent cardiovascular depression, but the severity of cardiac adverse events is generally low. However, propofol can induce vasodilation, which can be minimized by supplementing with IV fluids. Propofol can cause spontaneous muscle movements (paddling, tremors, muscle rigidity), panting, nystagmus, salivation, and retraction of tongue in some animals (incidence 3%-7%). Less frequent adverse reactions include vomiting during recovery and pain. Pain upon injection occurs in people but is less common in dogs. The pain from injection is caused by the free propofol in the formulation and is decreased with newer formulations. Phenolic drugs such as propofol may potentially cause oxidative damage to hemoglobin in cats because of higher concentration of oxidizable sulfhydryl groups in feline red blood cells (RBCs), leading to Heinz-body formation and methemoglobinemia. However, this has not been a consistent problem with routine clinical use, and repeated anesthetic episodes have been performed safely in cats. Some formulations may contain 2% benzyl alcohol (20 mg/mL), which can produce hematologic abnormalities in some animals. However, this ingredient did not cause additional morbidity or problems in cats compared to other formulations.

When used alone in horses, it can cause excitement, myotonus, and problems during recovery. Therefore, when used in horses, other sedatives are recommended.

### Contraindications and Precautions

Propofol can induce apnea, hypoxia, and cyanosis upon induction. Supplemental oxygen should be available to prevent adverse effects. Do not administer to hypotensive animals. When propofol has been used to sedate animals for intradermal skin testing, it may produce a greater number of positive reactions. Propofol should not be used alone for anesthesia in horses—combine with other sedatives or premedications.

### Drug Interactions

Propofol can be used with several other anesthetics and adjuncts safely. It has been mixed with thiopental sodium (2.5%) in a 1:1 mixture without loss of effectiveness. Propofol has been used with atropine, glycopyrrolate, acepromazine, xylazine, oxymorphone, halothane, and isoflurane without any interactions observed.

## Instructions for Use

Shake well before using. Use strict aseptic technique for administration. Propofol may be diluted in 5% dextrose, lactated Ringer's solution, and 0.9% saline but not to less than 2 mg/mL concentration. Delay in penetration to brain is approximately 3 minutes; therefore there is a delayed CNS effect during injection. When using with

other drugs (acepromazine, barbiturates, opiates, etc.), lower doses should be administered because premedications and other sedatives greatly reduce the propofol dose requirements. The reduction in dose when used with premedications and other sedatives is approximately 16%-20% in cats and 20%-30% in dogs. A mixture of 1:1 thiopental (2.5%) and propofol can be used in dogs and results in a smooth induction.

### Patient Monitoring and Laboratory Tests

Monitor respiration rate and character during anesthesia with propofol.

### Formulations

- The human formulation of propofol is available in 1% (10-mg/mL) injection in 20-mL ampules.
- The veterinary formulation is available in multidose vials containing 10 mg propofol per mL. Propofol is only slightly soluble in water; therefore it is formulated in a white, oil-in-water emulsion. It also contains soybean oil (100 mg/mL), glycerol (22.5 mg/mL), egg lecithin (12 mg/mL), and oleic acid (0.6 mg/mL) with sodium hydroxide to adjust the pH. The propofol emulsion is isotonic and has a pH of 6.0-9.0. **Note:** The formulation known as PropoClear emulsion for dogs and cats (without lipids) was associated with adverse reactions and has been removed from the market.

### Stability and Storage

Store between 4° and 25° C (40° and 77° F). Do not freeze. Protect from light. Shake well before use. The original formulation was available in an ampule without preservatives and had to be discarded within 6 hours. Use careful technique to prevent microbial contamination of this formulation. Newer formulations contain preservatives that allow for a 28-day shelf-life after opening the vial (PropoFlo 28 and PropoFlo Plus). Propofol has been mixed with thiopental sodium in a 1:1 mixture, and they are physically and chemically compatible. However, do not mix with other drugs unless compatibility is known. Propofol has a pH of 7-8.5. Protect from light. Store at 40° F-72° F (4° C-22° C). Do not freeze.

### Small Animal Dosage

#### Dogs

- 6.6 mg/kg IV slowly over 30-60 seconds. If necessary, an additional dose can be given at 0.5-1 mg/kg for intubation. Although the typical range needed for induction is 5-7 mg/kg IV, most inductions can be performed with 3.7 ( $\pm 1.5$ ) mg/kg. If premedicated with  $\alpha_2$ -agonists (e.g., dexmedetomidine) or other premedications, lower the dose by 20%-30% (e.g., lower dose of 3 mg/kg can be used). After initial induction, maintenance doses of 1-3 mg/kg IV can be used.
- CRI: 5 mg/kg slowly IV, followed by 100-400 mcg/kg/min (or 6-24 mg/kg/hour).
- Status epilepticus: 1-6 mg/kg IV (to effect), followed by CRI of 0.1-0.6 mg/kg/min.

#### Cats

- Anesthesia induction: 4-8 mg/kg IV slowly. After initial dose, incremental doses of 1-3 mg/kg IV can be administered as needed. If other preanesthetics and sedatives are used, reduce by 16%-24%. If combined with midazolam, the propofol requirement listed can be reduced by as much as 25%.
- CRI: 6 mg/kg slowly IV, followed by 200-300 mcg/kg/min (0.2-0.3 mg/kg) IV. For short-term procedures the total dose is 15 mg/kg for 30-minute protocol.
- CRI infusion with ketamine in cats: 0.025 mg/min/kg + ketamine 23-46 mcg/kg/min.
- Short-term surgery: 10 mg/kg IV dose delivered over 1 minute (duration of anesthesia 10-20 min).



## Large Animal Dosage

### Horses

- 2 mg/kg IV bolus. Guaifenesin (90 mg/kg IV) should be administered prior to propofol to prevent excitement and myotonus and other problems during recovery.

### Small Ruminants

- 4 mg/kg IV.

### Pigs

- 2-5 mg/kg IV.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

## Propranolol Hydrochloride

proe-pran'oh-lole hye-droe-klor'ide

**Trade and other names:** Inderal and generic brands

**Functional classification:** Beta blocker

## Pharmacology and Mechanism of Action

Beta-adrenergic blocker. Nonselective for  $\beta_1$ - and  $\beta_2$ -adrenergic receptors. Class II antiarrhythmic. Propranolol is a lipophilic beta blocker and relies on the liver for clearance. Lipophilic beta blockers such as propranolol undergo high first-pass clearance, which reduces oral bioavailability and causes high interpatient variability in plasma concentrations and effects. Drug concentrations may be higher when there is impaired liver blood flow.

## Indications and Clinical Uses

Propranolol is used primarily to decrease heart rate, decrease cardiac conduction, control tachyarrhythmias, and decrease blood pressure. It is effective in controlling the response from adrenergic stimulation. Beta blockers such as propranolol are among the most effective drugs for slowing heart rate.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects related to  $\beta_1$ -blocking effects on heart. Propranolol causes cardiac depression and decreases cardiac output.  $\beta_2$ -blocking effects can cause bronchoconstriction and decrease insulin secretion. Switch to a more specific  $\beta_1$ -blocker (see Instructions for Use below) if  $\beta_2$ -blocking effects are undesirable. Weakness and fatigue can be caused by beta blockers, which can indicate that a reduction in dose is needed.

### Contraindications and Precautions

Do not administer to animals with low cardiac reserve, bradycardia, or poor systolic function. Use cautiously in animals with respiratory problems; bronchoconstriction can occur from  $\beta_2$  effects. Hyperthyroid cats may have reduced clearance and increased risk of toxicity.

### Drug Interactions

Lipophilic beta blockers, such as propranolol, rely on the liver for clearance. These drugs are subject to interactions from drugs that affect liver blood flow and interact with hepatic enzymes. Decreased liver blood flow will reduce propranolol clearance.

### Instructions for Use

Usually dose is titrated according to patient's response. Start with a low dose and increase gradually to desired effect. Clearance relies on hepatic blood flow; use cautiously in animals with impaired hepatic perfusion. In cats with hyperthyroidism, consider reducing the dose to prevent adverse effects. Cats with hyperthyroidism may have decreased clearance or increased oral absorption compared with other cats. Propranolol is a non-specific beta-blocker. If a more specific blocker is needed (i.e., specific for the  $\beta_1$ -receptor) consider atenolol or metoproprolol, which are listed in other sections of this book.

### Patient Monitoring and Laboratory Tests

Monitor heart rate during treatment. Monitor respiratory function in patients prone to bronchoconstriction.

### Formulations

- Propranolol is available in 10-, 20-, 40-, 60-, and 80-mg tablets; 1-mg/mL injection; and 4- and 8-mg/mL oral solution.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Propranolol is soluble in water and ethanol. Suspensions prepared in various syrups and flavorings were stable for 4 months, but some settling may occur (shake before administration). pH of formulations should be kept at 2.8-4 for maximum stability. In alkaline solutions it will decompose.

### Small Animal Dosage

#### Dogs

- 20-60 mcg/kg over 5-10 min IV (titrate dose to effect).
- 0.2-1 mg/kg q8h PO (titrate dose to effect).

#### Cats

- 0.4-1.2 mg/kg (2.5-5 mg/cat) q8h PO.

### Large Animal Dosage

#### Horses

- 0.1 mg/kg IV slowly. Repeat in 6-8 hours if necessary. If low dose is not effective, administer 0.5 mg/kg and increase dose to 2 mg/kg IV gradually until desired response.
- 0.4-0.8 mg/kg q8h PO.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 3

## Propylthiouracil

pro-pil-thye-oh-yoo'rah-sil

**Trade and other names:** Propyl-Thyracil, PTU, and generic brands

**Functional classification:** Antithyroid

### Pharmacology and Mechanism of Action

Antithyroid drug. Propylthiouracil inhibits synthesis of thyroid hormones; specifically, it interferes with conversion of  $T_4$  to  $T_3$ .

### Indications and Clinical Uses

Propylthiouracil has been used for the treatment of feline hyperthyroidism. Because of adverse effects, use of propylthiouracil in most cats has been replaced with methimazole or carbimazole. The only remaining indication for propylthiouracil in animals is to treat an acute “thyroid storm” because it rapidly inhibits conversion of  $T_3$  to  $T_4$ , which methimazole does not.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects in cats include hepatopathy, hemolytic anemia, thrombocytopenia, and other signs of immune-mediated disease. If these signs are observed, the medication should be changed to another antithyroid agent.

#### Contraindications and Precautions

Do not use in cats with low platelet counts or bleeding problems.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Avoid the use of propylthiouracil because of the frequency of adverse effects. Other drugs can be used as a replacement, such as methimazole or carbimazole.

### Patient Monitoring and Laboratory Tests

Monitor CBC to look for evidence of hematologic abnormalities. Monitor  $T_4$  levels to assess therapy.

### Formulations

Propylthiouracil is available in 50- and 100-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Propylthiouracil is slightly soluble in water and soluble in ethanol.

### Small Animal Dosage

#### Cats

- 11 mg/kg q12h PO.

### Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Prostaglandin F<sub>2</sub> Alpha

pross-teh-glan'din

**Trade and other names:** Lutalyse, Dinoprost, and PGF<sub>2</sub> alpha

**Functional classification:** Prostaglandin

## Pharmacology and Mechanism of Action

Prostaglandin F<sub>2</sub> (PGF<sub>2</sub>) alpha simulates the action of endogenous PGF<sub>2</sub> alpha in animals. It induces luteolysis and will terminate pregnancy. It is also called dinoprost. The synthetic form is called cloprostenol (see cloprostenol section in this book for more information), which is often used in animals.

## Indications and Clinical Uses

PGF<sub>2</sub> alpha has been used to treat open pyometra in animals. In cattle, dinoprost has been used for treatment of chronic endometritis. Use for inducing abortion in small animals has been questioned, and other drugs are usually used instead. For example, synthetic PGF<sub>2</sub> alpha analogs such as cloprostenol are more potent with fewer adverse effects. However, in large animals, dinoprost is used to induce abortion in the first 100 days of gestation. It is used for estrous synchronization in cattle and horses by causing luteolysis. In pigs, dinoprost is used to induce parturition when given within 3 days of farrowing.

## Precautionary Information

### Adverse Reactions and Side Effects

PGF<sub>2</sub> alpha causes increased smooth muscle tone, resulting in diarrhea, abdominal discomfort, bronchoconstriction, and an increase in blood pressure. In small animals, other side effects include vomiting. Induction of abortion may cause retained placenta.

### Contraindications and Precautions

Do not administer intravenously. PGF<sub>2</sub> alpha induces abortion in pregnant animals. Use caution when handling this drug. It should not be handled by pregnant women. Absorption through the intact skin is possible. People with respiratory problems also should not handle dinoprost because absorption across the skin may lead to bronchoconstriction.

### Drug Interactions

According to the label, dinoprost should not be used with NSAIDs because these drugs inhibit synthesis of prostaglandins. However, NSAIDs should not affect concentrations of PGF<sub>2</sub> alpha after administration with this product. When using oxytocin concurrently, it should be used cautiously because there is a risk of uterine rupture.

## Instructions for Use

Use in treating pyometra should be monitored carefully.

## Patient Monitoring and Laboratory Tests

Monitor for signs of estrus after treatment.

## 690 Pseudoephedrine Hydrochloride

### Formulations

- PGF<sub>2</sub> is available in a 5-mg/mL solution for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. It should be stored in a manner to avoid skin contact with humans.

### Small Animal Dosage

#### Dogs

- Pyometra: 0.1-0.2 mg/kg once daily for 5 days SQ.
- Termination of pregnancy: 0.1-0.25 mg/kg q 8-12h, SC, or 0.1 mg/kg, q8h, SC for 2 days, then increase to 0.2 mg/kg q8h, SC until abortion is complete.

#### Cats

- Pyometra: 0.1-0.25 mg/kg once daily for 5 days SQ.
- Termination of pregnancy: 0.5-1 mg/kg IM for two injections.

### Large Animal Dosage

#### Cattle

- Termination of pregnancy: 25 mg total dosage, administered once IM.
- Estrus synchronization: 25 mg once IM or twice at 10- to 12-day intervals.
- Pyometra: 25 mg IM administered once.

#### Horses

- Estrus synchronization: 1 mg/100 pounds (1 mg/45 kg) IM or 1-2 mL administered once IM. Mares should return to estrus within 2-4 days and ovulate 8-12 days after treatment.

#### Pigs

- Induction of parturition: 10 mg administered once IM. Parturition occurs within 30 hours.

### Regulatory Information

No withdrawal time required for meat or milk.

## Pseudoephedrine Hydrochloride

soo-doh-eh-fed'rin hye-droe-klor'ide

**Trade and other names:** Sudafed and generic brands

**Functional classification:** Adrenergic agonist

### Pharmacology and Mechanism of Action

Adrenergic agonist. Pseudoephedrine is a sympathomimetic. It nonselectively acts as an agonist for the alpha-adrenergic and beta-adrenergic receptors. These receptors are found throughout the body, such as on sphincters, blood vessels, smooth muscle, and heart. Pseudoephedrine produces a similar effect as ephedrine and phenylpropanolamine. However, compared to ephedrine it may have fewer CNS effects.

### Indications and Clinical Uses

Pseudoephedrine has been used as a decongestant, as a mild bronchodilator, and to increase tone of urinary sphincter. Pseudoephedrine, phenylpropanolamine, and ephedrine have similar alpha-receptor and beta-receptor effects. The most common use in animals is for treating urinary incontinence. The mechanism for this action

appears to be via stimulating receptors on the sphincter. In people, it has been used as a decongestant. However, because pseudoephedrine is easily diverted to manufacture of methamphetamine, the availability in human medicine has diminished unless available by prescription. Most of the OTC forms and combination products for people have been removed. For animals, phenylpropanolamine will produce similar effects and may be substituted.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are attributed to adrenergic effects. These include excitement, rapid heart rate, increased blood pressure, and arrhythmias.

#### Contraindications and Precautions

Pseudoephedrine may cause some effects that are similar to phenylpropanolamine. Use cautiously in patients with cardiovascular disease. Use cautiously with drugs that are monoamine oxidase inhibitors (MAOI). Beta agonists such as pseudoephedrine may increase blood glucose. Pseudoephedrine has been used in clandestine laboratories to illegally manufacture methamphetamine. Therefore the availability of pseudoephedrine has been limited in most states.

#### Drug Interactions

Pseudoephedrine, like other sympathomimetic agents, is expected to potentiate other alpha- and beta-receptor agonists. It may cause increased vasoconstriction and changes in heart rate. Use cautiously with other vasoactive drugs. Use cautiously with other drugs that may lower seizure threshold. Use of inhalant anesthetics may increase cardiovascular risk. Do not use with tricyclic antidepressants (TCA) or monoamine oxidase inhibitors (MAOI).

### Instructions for Use

Although clinical trials have not been conducted for comparison, it is believed that the action and efficacy of pseudoephedrine are similar to ephedrine and phenylpropanolamine.

### Patient Monitoring and Laboratory Tests

Monitor heart rate in patients. If possible, monitor blood pressure and ECG in patients that may be susceptible to cardiovascular problems.

### Formulations Available

Pseudoephedrine has been available in 30- and 60-mg tablets, 120-mg capsules, and 6-mg/mL syrup, but availability of human formulations has diminished because of reasons cited above. (Some combination formulations have other ingredients such as antitussives or antihistamines.)

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Pseudoephedrine is soluble in water and ethanol. Keep compounded formulations at a low pH for maximum stability. Protect from freezing.

### Small Animal Dosage

#### Dogs

- 0.2-0.4 mg/kg (or 15-60 mg/dog) q8-12h PO.

### Large Animal Dosage

- No doses have been reported for large animals.

**Regulatory Information**

Because of abuse in humans, many forms are now Controlled Schedule V substances. Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 3

**Psyllium**

sill'ee-um

**Trade and other names:** Metamucil and generic brands**Functional classification:** Laxative**Pharmacology and Mechanism of Action**

Bulk-forming laxative. The action of psyllium is to absorb water and expand to provide increased bulk and moisture content to the stool, which encourages normal peristalsis and bowel motility. Psyllium also may have antilipidemia effects.

**Indications and Clinical Uses**

Psyllium is administered orally for treatment of constipation and bowel evacuation. In horses, it has been used for treating sand colic, but the effectiveness for this indication has not been shown.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects have not been reported in animals. Intestinal impaction can occur with overuse or in patients with inadequate fluid intake. In horses, it may be difficult to administer via stomach tube because it is prone to forming a gel when mixed with water.

**Contraindications and Precautions**

No contraindications are reported for animals.

**Drug Interactions**

No drug interactions have been reported in animals.

**Instructions for Use**

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

**Patient Monitoring and Laboratory Tests**

Psyllium may lower serum cholesterol measurements.

**Formulations**

- Psyllium is available as powder, usually 3.4 g/tsp.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats**

- 1 teaspoon/5-10 kg (added to each meal).

## Large Animal Dosage

### Horses

- Up to 1000 mg/kg per day PO via stomach tube or added to feed.

## Regulatory Information

No withdrawal times are necessary.

## Pyrantel Pamoate, Pyrantel Tartrate

pye-ran'tel

**Trade and other names:** Nemex, Strongid, Priex, Pyran, and Pyr-A-Pam

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Antiparasitic drug. Pyrantel is in the class of tetrahydropyrimidines. Others in this class include morantel. Pyrantel acts to interfere with ganglionic neurotransmission via blocking with acetylcholine receptors and other sites. This causes paralysis of the parasites. Paralyzed worms are expelled from the intestinal lumen by peristalsis. Pyrantel is poorly water soluble and not absorbed systemically in ruminants, although some absorption occurs in monogastric animals. Most of the activity is confined to the intestinal lumen.

## Indications and Clinical Uses

Pyrantel is indicated for treatment of intestinal nematodes. In horses, it is used for treatment and prevention of nematodes, including pinworms (*Oxyuris equi*), large roundworms (*Parascaris equorum*), large strongyles (*Strongylus edentatus*, *S. equinus*, and *S. vulgaris*), and small strongyles. When added to medicated feed, it is used to control nematodes, including pinworms (*O. equi*), large roundworms (*P. equorum*), large strongyles (*S. edentatus*, *S. vulgaris*, and *Triodontophorus* species), and small strongyles. In pigs, it is used for prevention of large roundworm (*Ascaris suum*) and prevention of the nodular worm *Oesophagostomum* spp. In dogs and cats, it is used for treatment of nematodes, including hookworms (*Ancylostoma* spp.) and roundworms (*Toxocara cati*, *T. canis*, and *Toxascaris leonina*). There is some evidence that it is effective for control of some tapeworms, but ordinarily other drugs should be used for tapeworms.

## Precautionary Information

### Adverse Reactions and Side Effects

No adverse effects reported.

### Contraindications and Precautions

No contraindications in animals. It may be used in all ages and in lactating and pregnant animals.

### Drug Interactions

Central nervous system toxicity may be more likely when coadministered with levamisole, but this is not reported from clinical use in animals.



**Instructions for Use**

Shake suspension prior to use. Doses listed are for single dose, but they may be repeated as part of a parasite management program. Lower doses may be added to daily feed for prevention of parasites.

**Patient Monitoring and Laboratory Tests**

Monitor fecal samples for presence of intestinal parasites.

**Formulations**

- Pyrantel is available in 171-, 180-, and 226-mg (base) per mL paste; 22.7- and 113.5-mg (base) tablets; and 2.27-, 4.54-, and 50-mg (base) per mL suspension. Equine paste is 19.31%. It is also available in 10.6-, 12.6-, and 21.1-g/kg of pellets for medicated feed.
- Pyrantel pamoate is a salt and contains 34.7% pyrantel base. Doses are based on the amount of pyrantel base. Pyrantel tartrate contains 57.9% pyrantel base. Many of the formulations contain other antiparasitic drugs (e.g., praziquantel). For example, it is available as 13.6 mg praziquantel and 54.3 mg pyrantel, or 18.2 mg praziquantel and 72.6 mg pyrantel, or 27.2 mg praziquantel and 108.6 mg pyrantel.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Protect from freezing.

**Small Animal Dosage****Dogs**

- 5 mg/kg once PO; repeat in 7-10 days.

**Cats**

- 20 mg/kg once PO.
- Doses may be mixed with food.

**Large Animal Dosage****Horses**

- Nematodes: 6.6 mg/kg PO.
- Cestodes: 13.2 mg/kg.
- Medicated feed: 12.5 mg/kg as a single dose or 2.6 mg/kg/day for prevention.

**Pigs**

- 22 mg/kg administered in feed as a single treatment.

**Regulatory Information**

Pigs: 1-day withdrawal (US); 7 days (Canada).

Withdrawal times for other species are not established. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Pyridostigmine Bromide**

peer-id-oh-stig'meen broe'mide

**Trade and other names:** Mestinon and Regonol

**Functional classification:** Anticholinesterase, antimyasthenic

## Pharmacology and Mechanism of Action

Cholinesterase inhibitor and antimuscarinic drug. This drug inhibits the enzyme that breaks down acetylcholine. Therefore it prolongs the action of acetylcholine at the synapse. The major difference between physostigmine and neostigmine or pyridostigmine is that physostigmine crosses the blood-brain barrier and the others do not. Compared to neostigmine, pyridostigmine has a longer duration of action.

## Indications and Clinical Uses

Pyridostigmine is used as an antidote for anticholinergic intoxication and treatment (antidote) for neuromuscular blockade. It is also used as a treatment of myasthenia gravis, ileus, and retention of urine (such as postoperative) by increasing tone of bladder smooth muscle. Most often, pyridostigmine is the first drug of choice for myasthenia gravis and is preferred over neostigmine.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are caused by the cholinergic action resulting from inhibition of cholinesterase. These effects can be seen in the gastrointestinal tract as diarrhea and increased secretions. Other adverse effects can include miosis, bradycardia, muscle twitching or weakness, and constriction of bronchi and ureters. Pyridostigmine may be associated with fewer adverse effects than neostigmine, but the effects of pyridostigmine may persist longer. If adverse effects are observed, treat with anticholinergic drugs, such as 0.125 mg of hyoscyamine sulfate. Atropine also may be used.

#### Contraindications and Precautions

Do not use in these conditions: urinary obstruction, intestinal obstruction, asthma or bronchoconstriction, pneumonia, and cardiac arrhythmias. Do not use in patients sensitive to bromide. Consider the amount of bromide in dose in any patient also receiving bromide (KBr) for treatment of seizures.

#### Drug Interactions

Bromide concentration in the formulation should be considered for animals also receiving bromide (e.g., potassium bromide) for treatment of epilepsy. (Sodium bromide may be used as an alternative.)

## Instructions for Use

Pyridostigmine is used for treatment of myasthenia gravis. Neostigmine and pyridostigmine have fewer side effects than physostigmine. When used, frequency of dose may be increased based on observation of effects. After administration, pyridostigmine benefits should be observed in approximately 15-30 minutes. The duration of action may be 3-4 hours.

## Patient Monitoring and Laboratory Tests

Monitor gastrointestinal effects. Monitor cardiac rate and rhythm.

## Formulations

Pyridostigmine is available in 12-mg/mL oral syrup, 60-mg tablets (scored), and 5-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Pyridostigmine is soluble in water. Store in acid solutions; it may decompose in alkaline vehicles.

**Small Animal Dosage****Dogs**

- Antimythasthenic: 0.02-0.04 mg/kg q2h IV or 0.5-3 mg/kg q8-12h PO.
- Antidote for muscle blockade: 0.15-0.3 mg/kg IM or IV as needed.

**Cats**

- 0.1-0.25 mg/kg q24h PO. CRI: 0.01-0.03 mg/kg/hour IV.

**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

**Pyrimethamine**

peer-ih-meth'ah-meen

**Trade and other names:** Daraprim

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Antibacterial and antiprotozoal drug. Pyrimethamine blocks the dihydrofolate reductase enzyme, which inhibits synthesis of reduced folate and nucleic acids. Activity of pyrimethamine is more specific against protozoa than bacteria. Pyrimethamine is often combined with a sulfonamide to produce a synergistic effect.

**Indications and Clinical Uses**

Pyrimethamine is used to treat protozoal infections in animals. It is most often combined with a sulfonamide, either separately or in a combined formulation. See [pyrimethamine](#) + sulfadiazine monograph in this book for additional information.

**Precautionary Information****Adverse Reactions and Side Effects**

There is a risk of folic acid anemia when pyrimethamine and sulfonamide combinations are administered. This has been observed in 12% of treated horses in a field trial. Folic or folinic acid (preferably folinic acid) has been supplemented to prevent anemia, but benefit of this treatment is unclear. Bone marrow suppression usually resolves after discontinuation of treatment. Diarrhea may occur after oral administration.

**Contraindications and Precautions**

Use cautiously in pregnant animals.

**Drug Interactions**

Drug interactions are not reported for animals. However, a combination of pyrimethamine with trimethoprim/sulfonamides will enhance the bone marrow toxicity.

## Instructions for Use

Pyrimethamine is used either alone or in combination with sulfonamides. (See [pyrimethamine](#) + sulfadiazine combination in this book for further details.)

## Patient Monitoring and Laboratory Tests

Monitor CBC periodically in animals receiving treatment.

## Formulations

- Pyrimethamine is available in 25-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Pyrimethamine is poorly soluble in water, but it is more soluble in ethanol. Tablets have been crushed to make extemporaneous suspensions in syrups and other flavorings. These formulations have been stable for 7 days and up to 90 days, depending on the formulation.

## Small Animal Dosage

### Dogs

- 1 mg/kg q24h PO for 14-21 days (5 days for *Neospora caninum*).

### Cats

- 0.5-1 mg/kg q24h PO for 14-28 days.

## Large Animal Dosage

- Horses, EPM caused by *Sarcocystis neurona*: 1 mg/kg q24h PO in combination with a sulfonamide (see details on [pyrimethamine](#) + sulfadiazine).

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Pyrimethamine and Sulfadiazine

peer-ih-meth'ah-meen and sul-fa-dye'ah-zeen

**Trade and other names:** ReBalance

**Functional classification:** Antiprotozoal

## Pharmacology and Mechanism of Action

Antibacterial, antiprotozoal drug, and sulfonamide combination. Pyrimethamine blocks dihydrofolate reductase enzyme, which inhibits synthesis of reduced folate and nucleic acids. Activity of pyrimethamine is more specific against protozoa than bacteria. Sulfadiazine provides a false PABA substrate for synthesis of dihydrofolic acid by bacteria and protozoa. Together the combination is synergistic against protozoa.

## Indications and Clinical Uses

Pyrimethamine + sulfadiazine is used to treat horses with equine protozoal myeloencephalitis (EPM). Although not approved for use to treat other animals, the equine formulation has been administered to small animals to treat protozoal infections caused by *Toxoplasma*, *Neospora*, and *Sarcocystis* species.

## Precautionary Information

### Adverse Reactions and Side Effects

In horses, at high doses, decreased blood count has been observed, but without evidence of anemia. Although anemia is possible, it resolves after discontinuing medication. Folic or folinic acid has been supplemented to prevent anemia, but benefit of this treatment is unclear. Because this combination contains a sulfonamide, adverse effects are possible. Multiple adverse effects have been documented from administration of sulfonamides. These include allergic reactions, Type II and III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites.

### Contraindications and Precautions

Do not administer to animals that may be prone to anemia or in which a CBC cannot be monitored. Do not administer to animals with a history of sensitivity to sulfonamides.

### Drug Interactions

Drug interactions are not reported for animals. However, a combination of pyrimethamine with trimethoprim/sulfonamides will enhance the bone marrow toxicity.

## Instructions for Use

Use of pyrimethamine/sulfadiazine has been primarily for treatment of protozoal infections in horses. However, there is anecdotal evidence that pyrimethamine + sulfadiazine may be indicated for treatment of some protozoa (e.g., *Toxoplasma*, *Neospora*, or *Sarcocystis*) in small animals.

## Patient Monitoring and Laboratory Tests

Monitor CBC periodically in animals receiving treatment. A CBC should be performed at least monthly in treated animals.

## Formulations

- Pyrimethamine + sulfadiazine is available in an oral suspension for horses that is 250 mg sulfadiazine and 12.5 mg pyrimethamine per mL.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Do not freeze.

## Small Animal Dosage

### Dogs and Cats

- 1 mg/kg pyrimethamine and 20 mg/kg sulfadiazine once daily PO. (Equivalent to one-third milliliter (0.33 mL) of the equine formulation per 4 kg of body weight.)

## Large Animal Dosage

- EPM caused by *S. neurona*: 1 mg/kg pyrimethamine, 20 mg/kg sulfadiazine q24h PO (4 mL per 110 pounds). Treatment duration in horses varies from 90-270 days.

## Regulatory Information

Do not administer to animals intended for food.

## Quinacrine Hydrochloride

kwin'eh-krin hye-droe-klor'ide

**Trade and other names:** Atabrine (No longer available in the US.)

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Antimalarial drug. Quinacrine is an outdated antimalarial drug. It inhibits nucleic acid synthesis in parasites.

### Indications and Clinical Uses

Quinacrine is used occasionally for treatment of protozoa (*Giardia*), but other drugs (e.g., metronidazole and tinidazole) are used more often. Although it is not commercially available, veterinarians have obtained quinacrine through compounding pharmacies.

### Precautionary Information

#### Adverse Reactions and Side Effects

Side effects are common. Vomiting occurs after oral administration.

#### Contraindications and Precautions

No contraindications are reported for animals.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Doses listed are for treatment of giardiasis. Effects for other organisms are not reported.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Quinacrine has been available in 100-mg tablets. Quinacrine may no longer be marketed in the US, but it may be available from some pharmacies in a compounded formulation.

### Stability and Storage

Store in a tightly closed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 6.6 mg/kg q12h PO for 5 days.

#### Cats

- 11 mg/kg q24h PO for 5 days.

### Large Animal Dosage

- No doses have been reported for large animals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

## Quinidine, Quinidine Sulfate

kwin-ih-deen

**Trade and other names:** Quinidine gluconate: Duraquin and Quinidine polygalacturonate: Cardioquin, and Quinidine sulfate: Cin-Quin, and Quinora

**Functional classification:** Antiarrhythmic

### Pharmacology and Mechanism of Action

Antiarrhythmic drug. Class I antiarrhythmic. Like other Class I antiarrhythmic drugs, its action is to inhibit sodium influx via blockade of sodium channels. Therefore it suppresses cardiac Phase 0 action potential and decreases ectopic arrhythmic foci.

### Indications and Clinical Uses

Quinidine is used to treat ventricular arrhythmias and occasionally to convert atrial fibrillation to sinus rhythm. In small animals, it is rarely used because other more effective and safer alternatives are available. For example, an oral alternative for dogs is mexiletine. In horses and cattle, quinidine has been the drug of choice to treat atrial fibrillation. However, other alternatives are considered because of frequency of adverse effects in horses and decreased availability of commercial forms of quinidine. Alternatives include diltiazem and electrical cardioversion.

### Precautionary Information

#### Adverse Reactions and Side Effects

Side effects with quinidine are more common than procainamide and include nausea and vomiting. Adverse effects include hypotension and tachycardia (because of vagolytic effect). With IV dosing, adverse effects such as hypotension and tachyarrhythmias are common in cattle. In horses, adverse effects are common, which include hypotension, gastrointestinal problems, and supraventricular tachycardia. Sudden cardiac death is possible but uncommon in horses.

#### Contraindications and Precautions

Quinidine may increase heart rate. Use cautiously in animals with heart disease.

#### Drug Interactions

Quinidine is a well-known multidrug resistance (ABCB1, also known as MDR1) membrane pump (P-glycoprotein) inhibitor. It will interfere with membrane channels and increase concentrations of some coadministered drugs. Coadministration with digoxin may increase digoxin concentrations. See Appendix K for list of potential p-glycoprotein substrates.

### Instructions for Use

Quinidine has a rapid clearance in cattle (half-life is 2.25 hours), which results in the need for frequent administration. Equine doses are usually administered orally via stomach tube. Because of decreased availability of commercial forms and frequency of adverse effects, quinidine is not used as commonly as other Class I antiarrhythmic drugs. If quinidine is administered, calculate the dose to the amount of quinidine base in each formulation: 324 mg of quinidine gluconate has a 202-mg quinidine base; 275 mg of quinidine polygalacturonate has a 167-mg quinidine base; 300 mg of quinidine sulfate has a 250-mg quinidine base.

## Patient Monitoring and Laboratory Tests

Quinidine can be hypotensive and vagolytic. Monitor patient's electrocardiogram (ECG) for arrhythmias and monitor blood pressure.

## Formulations

- In some countries, quinidine is being discontinued and may be difficult to obtain. Older formulations include quinidine gluconate 324-mg tablets and 80-mg/mL injection; quinidine polygalacturonate in 275-mg tablets; and quinidine sulfate in 100-, 200-, and 300-mg tablets, 200- and 300-mg capsules, and 200-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Quinidine is slightly soluble in water. Quinidine salts may form a dark color when exposed to light and should not be used. Quinidine has been compounded for oral use in syrups (e.g., Ora Sweet) and is stable for 60 days.

## Small Animal Dose

### Dogs

- Quinidine gluconate: 6-20 mg/kg q6h IM or 6-20 mg/kg q6-8h PO (of base).
- Quinidine polygalacturonate: 6-20 mg/kg q6h PO (of base).
- Quinidine sulfate: 6-20 mg/kg q6-8h PO (of base) or 5-10 mg/kg q6h IV.

## Large Animal Dosage

### Cattle

- Treatment of atrial fibrillation: Quinidine is poorly absorbed orally in cattle and must be given IV. A loading dose of 49 mg/kg (given over 4 hours) to be followed by 42 mg/kg IV maintenance dose. Or give 40 mg/kg diluted in 4 L of fluid slowly at a rate of 1 L/hr until fibrillation is converted.

### Horses

- Atrial fibrillation treatment (usually orally with a stomach tube): 5 grams per 450 kg body weight (per 1000 pounds) for the first treatment; thereafter give 10 grams per 450 kg every 2 hours until the sinus rate is achieved. IV dose is 1-1.5 mg/kg every 10-15 min to a total dose of 10 mg/kg or until sinus rate conversion.

## Regulatory Information

Withdrawal times are not established for animals that produce food. Because of rapid elimination, short withdrawal times can be used. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Racing Commissioners International (RCI) Classification: 4



## Racemethionine

rah-see'meth-eye'oh-neen

**Trade and other names:** Methio-Form, and generic brands and Pedameth, Uracid, and generic brands (human preparations)

**Functional classification:** Acidifier

### Pharmacology and Mechanism of Action

Urinary acidifier. Methionine lowers urinary pH. Racemethionine also has been used to protect against acetaminophen overdose in people by restoring hepatic concentrations of glutathione.

### Indications and Clinical Uses

It is used as a urinary acidifier. In people, it also is used to treat dermatitis caused by urinary incontinence (reduces urine ammonia).

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported.

#### Contraindications and Precautions

Do not use in animals with metabolic acidosis. Do not use in young cats. Do not use in animals with hepatic disease.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Use for acetaminophen toxicity has been replaced by acetylcysteine.

### Patient Monitoring and Laboratory Tests

Monitor complete blood count (CBC) and hepatic enzymes if used to treat toxicity.

### Formulations

- Racemethionine is available in 500-mg tablets, 75-mg/5-mL pediatric oral solution, 200-mg capsules, and powders to add to an animal's food.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 150-300 mg/kg/day PO.

#### Cats

- 1-1.5 g per cat PO (added to food each day).

### Large Animal Dosage

- No doses have been reported for large animals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

## Ramipril

ram'ih-pril

**Trade and other names:** Vasotop

**Functional classification:** Vasodilator, angiotensin-converting enzyme (ACE) inhibitor

### Pharmacology and Mechanism of Action

Ramipril is an angiotensin converting enzyme (ACE) inhibitor. Like other ACE inhibitors, ramipril inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and will stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The ability of aldosterone to cause sodium and water retention contributes to congestion. Ramipril, like other ACE inhibitors, will cause vasodilation and decrease aldosterone-induced congestion. Angiotensin-converting enzyme inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins. There is evidence for a cardioprotective effect when used to treat dogs with heart disease caused by cardiomyopathy or valvular disease.

### Indications and Clinical Uses

Ramipril is used to treat hypertension and congestive heart failure (CHF). It has not been studied as much as other ACE inhibitors in animals (e.g., enalapril or benazepril), but it is expected to have similar pharmacodynamic effects. Because no ACE inhibitor has been shown to be superior to another, there is little reason to use ramipril instead of enalapril or benazepril in dogs or cats. It has been primarily used in dogs. It has also been used safely in cats to control hypertension, but has not been effective for treating hypertrophic cardiomyopathy.

### Precautionary Information

#### Adverse Reactions and Side Effects

It has not been used as often as other drugs in this class; therefore a full range of potential adverse effects has not been reported. Ramipril was well tolerated in clinical studies in dogs.

#### Contraindications and Precautions

Studies performed in experimental dogs indicated that dose adjustments are not necessary when administering ramipril in dogs with impaired kidney function. However, as with any ACE inhibitor, monitor patients carefully if they have renal insufficiency or decreased glomerular filtration rate (GFR) that could be impaired with ACE inhibitor treatment. Discontinue use of ACE inhibitors in pregnant animals; they cross the placenta and have caused fetal malformations and death of the fetus.

#### Drug Interactions

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease vasodilating effects.

### Instructions for Use

Clinical efficacy has been demonstrated in dogs with dilated cardiomyopathy. Other drugs used for treatment of heart failure may be used concurrently. Dogs also may receive pimobendan, digoxin, and/or furosemide with ramipril.

### **Patient Monitoring and Laboratory Tests**

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

### **Formulations**

- Ranipril is available in 1.25-, 2.5-, 5-, and 10-mg capsules.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

### **Small Animal Dosage**

#### **Dogs**

- 0.125-0.25 mg/kg daily PO to a maximum of 0.5 mg/kg per day.

#### **Cats**

- 0.125 mg/kg q24h PO.

### **Large Animal Dosage**

- No doses have been reported for large animals.

### **Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## **Ranitidine Hydrochloride**

rah-nit'ih-deen hye-droe-klor'idē

**Trade and other names:** Zantac

**Functional classification:** Antilucer agent

### **Pharmacology and Mechanism of Action**

Histamine<sub>2</sub>-antagonist (H<sub>2</sub>-blocker). Ranitidine, like other H<sub>2</sub> blockers, suppresses histamine stimulation of gastric parietal cells to decrease gastric acid secretion. Ranitidine will increase stomach pH. It is longer acting and 4 to 10 times more potent than cimetidine. The half-life of ranitidine is longer than cimetidine, which results in decreased frequency of administration for ranitidine. In horses, the half-life after IV and oral administration was 2.8 and 1.4 hours, respectively. The oral absorption in horses is 27%. In dogs, the half-life was 2.3 and 2.2 hours after oral and IV administration, respectively, with 95% oral absorption. By contrast, the half-life of cimetidine in dogs is 1.4 hours. When adjusting doses, ranitidine hydrochloride is 81% ranitidine.

### **Indications and Clinical Uses**

Ranitidine is used to treat ulcers and gastritis. It does not produce as much of a sustained increase in stomach pH as proton pump inhibitors (omeprazole). Proton pump inhibitors such as omeprazole have been preferred in dogs, cats, and horses for sustained suppression of gastric acid secretion for healing and preventing ulcers. Doses that maintained stomach pH in the range to prevent ulcers in dogs may be much higher than the doses used clinically. Ranitidine (6.6 mg/kg PO) in foals suppressed acid for 6 hours, but omeprazole suppressed acid for 22 hours at 4 mg/kg. Ranitidine has been used to prevent NSAID-induced ulcers in animals, although efficacy has not been demonstrated for this effect. In horses, ranitidine did not improve

healing of ulcers induced by NSAIDs, and it was not as effective as omeprazole for treating ulcers. Ranitidine may stimulate stomach emptying and colon motility via anticholinesterase action. In horses, the effect on gastric emptying is minimal.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are usually seen only with decreased renal clearance. In people, central nervous system (CNS) signs may occur with high doses. Ranitidine may have fewer effects on endocrine function and drug interactions compared to cimetidine.

#### Contraindications and Precautions

Fewer drug interactions are possible with ranitidine compared with cimetidine because ranitidine does not inhibit cytochrome P450 enzymes.

#### Drug Interactions

Ranitidine and other H<sub>2</sub>-receptor blockers block secretion of stomach acid. Therefore they will interfere with oral absorption of drugs dependent on acidity, such as ketoconazole, itraconazole, and iron supplements. Unlike cimetidine, ranitidine is not known to inhibit microsomal P450 enzymes.

### Instructions for Use

Pharmacokinetic information in dogs suggests that ranitidine may be administered less often than cimetidine to achieve continuous suppression of stomach acid secretion. However, ranitidine may be less effective in dogs and cats to produce effective suppression of stomach acid secretion than previously thought. Use in horses and foals is based on experimental studies and pharmacokinetic data and is less effective than omeprazole.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Ranitidine is available in 75-, 150-, and 300-mg tablets; 150- and 300-mg capsules; and 25-mg/mL injection. Some forms are available over-the-counter (OTC).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Ranitidine hydrochloride is soluble in water. Tablets have been crushed and mixed with water and syrup and were stable for 7 days. Protect from freezing.

### Small Animal Dosage

#### Dogs

- 2 mg/kg q8h IV or PO.

#### Cats

- 2.5 mg/kg q12h IV or 3.5 mg/kg q12h PO.

### Large Animal Dosage

#### Horses

- 2.2-6.6 mg/kg q6-8h PO. The higher dose (6.6 mg/kg) is more effective at suppressing stomach acid.
- 2 mg/kg q6-8h IV.

#### Calves

- 50 mg/kg q8h PO in milk-fed calves.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). Racing Commissioners International (RCI) Classification: 5

**Remifentanyl Hydrochloride**

Rem-i-fen'ta-nil

**Trade and other names:** Ultiva

**Functional classification:** Anesthetic, analgesic, opioid

**Pharmacology and Mechanism of Action**

Remifentanyl is an opioid similar in potency and activity to fentanyl. Like fentanyl, remifentanyl has activity primarily at the mu-opiate receptor. The difference between remifentanyl and other opioids is that it has an ultrashort action. The rapid onset and peak effect and short duration of action are attributed to its unique disposition. Remifentanyl is quickly metabolized by hydrolysis of the propanoic acid-methyl ester by blood and tissue esterases. Therefore it is rapidly metabolized in the blood, does not depend on liver metabolism, and can be used safely in patients with liver or kidney disease. It also is rapidly delivered to tissues with a high octanol:water partition coefficient of 17.9 at pH 7.3. However, it does not accumulate in tissues or blood even after prolonged IV infusions. Because of the rapid metabolism and quick equilibration between plasma and tissues, remifentanyl has a fast onset of activity after IV injection. The half-life in dogs is approximately 3-6 minutes and does not change with increasing doses. Recovery occurs rapidly (within 5-10 minutes), and when using constant-rate infusions (CRIs), new steady-state concentrations can be achieved within 5-10 minutes after changes in infusion rate. Because of rapid equilibration with tissues, it can be easily titrated to the desired depth of anesthesia/analgesia by changing the continuous infusion rate or by administering an IV bolus injection.

**Indications and Clinical Uses**

Remifentanyl is used for induction and maintenance of anesthesia, often in combination with other agents. Because of its rapid metabolism and short half-life, it should be administered via CRI to maintain a balanced anesthetic effect. It can be administered with other drugs, including inhalant anesthetics, propofol, alpha<sub>2</sub>-agonists, sedatives, and tranquilizers. Because it does not require hepatic metabolism or renal elimination, it can be administered safely to patients that have liver or kidney disease. Remifentanyl use in dogs is limited to a few studies and case reports. Doses in animals have been extrapolated from humans (human starting dose is 0.1 mcg/kg/min CRI). Remifentanyl has been infused safely in cats, and over a wide range of doses (0.06-16 mcg/kg/min) IV it did not affect isoflurane minimum alveolar concentration (MAC).

**Precautionary Information****Adverse Reactions and Side Effects**

Like other opioids and opiates, remifentanyl has adverse effects that are attributed to the binding to opiate receptors. These effects include reduced heart rate and sedation. In people, at rates greater than 0.2 mcg/kg/min, respiratory depression

occurs. In cats, remifentanyl induced dysphoria at high infusion rates ( $>8$  mcg/kg/min). Adverse effects will quickly dissipate when the infusion is discontinued because of the drug's rapid metabolism in the plasma and tissues. The opioid activity of remifentanyl is antagonized by opioid antagonists such as naloxone.

### Contraindications and Precautions

Remifentanyl will potentiate the effects of other anesthetics. Use cautiously in animals sensitive to opiates. It is intended for IV administration only. Do not administer via epidural, intrathecal, intradermal, IM, or SQ routes.

### Drug Interactions

Other anesthetics will be potentiated when used with remifentanyl. Lower doses of other anesthetic agents may be used when combined with remifentanyl.

## Instructions for Use

Administer intravenously as a CRI. A bolus dose may be administered prior to the start of the CRI.

## Patient Monitoring and Laboratory Tests

Monitor patients during anesthetic protocol. Monitor electrocardiogram (ECG), heart rate, and breathing character.

## Formulations

- Remifentanyl is available in a 1-mg/mL solution and in vials of 1, 2, or 5 mg of remifentanyl base. Add 1 mL of diluent per milligram of remifentanyl to produce a solution of 1 mg/mL. This solution can be further diluted for IV use to a concentration of 20, 25, 50, or 250 mcg/mL.

## Stability and Storage

The vial is available in a lyophilized powder that must be reconstituted prior to use. Store powder for injection in refrigerator ( $36^{\circ}$ - $46^{\circ}$  F) or at room temperature (less than  $78^{\circ}$  F). Remifentanyl HCl has a pKa of 7.07, but the pH of reconstituted solutions ranges from 2.5-3.5. The pH of solutions should be considered when combining with other drugs or fluid solutions. Remifentanyl is compatible with sterile water, lactated Ringer's solution, 5% dextrose, 0.9% sodium chloride, and 0.45% sodium chloride. Once mixed in solution, it is stable for 24 hours at room temperature. It can also be mixed in solution with propofol. Because of the presence of plasma esterases, it should not be mixed with blood products. Therefore administration with IV blood transfusions is not recommended.

## Small Animal Dosage

### Dogs

- CRI: 0.20 mcg/kg/min, up to 1 mcg/kg/min. Infusion rate can be adjusted to achieve desired effect, but 0.30 mcg/kg/min was optimum to achieve desired effects in anesthetized dogs, and higher rates did not produce increased benefit.

### Cats

- 2.5 mcg/kg bolus injection followed by 0.2-0.24 mcg/kg/minute CRI. (Similar infusion rates have been used as in dogs.)

## Large Animal Dosage

- No doses have been reported for large animals.

**Regulatory Information**

Remifentanyl is a Schedule II controlled substance. Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Riboflavin (Vitamin B<sub>2</sub>)**

rye'boe-flay-vin

**Trade and other names:** Vitamin B<sub>2</sub>**Functional classification:** Vitamin**Pharmacology and Mechanism of Action**

Vitamin B<sub>2</sub> supplement. Thiamine is commonly included as an ingredient in vitamin B complex aqueous solutions for injection. In these formulations it is available as 5' phosphate sodium riboflavin. Vitamin B complex often contains thiamine (B<sub>1</sub>), riboflavin, niacinamide, and cyanocobalamin B<sub>12</sub>.

**Indications and Clinical Uses**

Riboflavin is used as a vitamin B<sub>2</sub> supplement. It is usually administered for maintenance in patients who are vitamin B<sub>2</sub> deficient.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are rare because water-soluble vitamins are easily excreted. Riboflavin may discolor the urine.

**Contraindications and Precautions**

Do not administer injectable solution by IV rapidly if it contains thiamine (vitamin B<sub>12</sub>) because this may cause an anaphylactic reaction.

**Drug Interactions**

No drug interactions have been reported in animals.

**Instructions for Use**

It is not necessary to supplement in animals with well-balanced diets.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Riboflavin is available in various-sized tablets in increments from 10-250 mg. Riboflavin is most commonly formulated with other vitamins in a "vitamin B complex" aqueous solution for injection (2 and 5 mg/mL of riboflavin).

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs**

- 10-20 mg/day PO.
- 1-4 mg/dog q24h SQ.

**Cats**

- 5-10 mg/day PO.
- 1-2 mg/cat q24h SQ.

## Large Animal Dosage

### Lambs

- 2-4 mg q24h IM or SQ.

### Calves and Foals

- 6-10 mg q24h IM or SQ.

### Cattle and Horses

- 20-40 mg q24h IM or SQ.

### Sheep and Pigs

- 10-20 mg q24h IM or SQ.

## Regulatory Information

Because of the low risk of harmful residues in animals intended for food, no withdrawal time is necessary.

## Rifampin

rih-fam'pin

**Trade and other names:** Rifadin, Rimactane, and Rifampicin

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Antibacterial. Action of rifampin is to inhibit bacterial RNA synthesis. Rifampin is a semisynthetic antibiotic derived from rifamycin B to produce rifampin (US and Canadian name), also known as rifampicin in Europe. Rifampin has a high activity against gram-positive bacteria (*Staphylococcus* spp.), *Mycobacterium* spp., *Haemophilus* spp., *Neisseria* spp., and *Chlamydia* spp. but more limited activity against the gram-negative bacteria because it penetrates the gram-positive organism cell wall more easily than the gram-negative organism cell wall. Rifampin is highly lipid soluble and has the characteristic of entering cells to concentrate in leukocytes to inhibit intracellular bacteria. This is a therapeutic advantage for treating intracellular organisms (*Brucella*, *Mycobacterium*, *Rhodococcus*, *Chlamydia*) and chronic granulomatous diseases. Rifampin enters the microbial cell and forms stable complexes with the beta subunit of DNA-dependent RNA polymerases of microorganisms. This binding results in inactive enzymes and inhibition of RNA synthesis by preventing chain initiation. Resistance occurs via a single mutation of the amino acid sequence of the beta subunit of the DNA-dependent RNA polymerase enzyme. Rifampin is rapidly absorbed from the gastrointestinal tract after oral administration in humans, dogs, calves, horses, and foals. Pharmacokinetics in adult horses shows rapid oral absorption of rifampin and a half-life of approximately 5-7 hours and a volume of distribution (VD) of 0.7 L/kg, but the half-life is longer in foals, at approximately 18 hours. The half-life in dogs is approximately 8 hours.

## Indications and Clinical Uses

Rifampin is used in people primarily for treatment of tuberculosis. In veterinary medicine, rifampin has been used to treat susceptible gram-positive and intracellular bacteria, including *Staphylococcus* species (including methicillin-resistant strains); *Streptococcus* spp.; *Rhodococcus equi*; *Corynebacterium pseudotuberculosis*; and most strains of *Bacteroides* spp., *Clostridium* spp., *Neisseria* spp., and *Listeria* spp. Gram-negative organisms are not affected at typical doses. In small animals, the most common use is to treat staphylococcal infections, particularly methicillin-resistant strains. Resistance among bacteria (e.g. *Staphylococcus* spp.) may develop, but this occurrence is generally not common and should not prevent its use in animals. One of the most common uses of rifampin is for treating infections caused by *R. equi* in horses. For



this treatment, it is frequently combined with erythromycin, azithromycin, or clarithromycin. Rifampin also may have activity against bacteria in biofilms. However, there are insufficient reports to confirm the clinical effectiveness for treating biofilm bacteria.

## Precautionary Information

### Adverse Reactions and Side Effects

In people, hypersensitivity and flulike symptoms are reported. Hepatotoxicity is seen more commonly in dogs when high doses are administered (10 mg/kg and higher). Hepatic enzyme elevations may be observed. In one study, adverse effects occurred in 16% of treated dogs (vomiting, anorexia, diarrhea) and 27% had reversible elevations of liver enzymes. When treating dogs, clinicians are advised to check liver enzymes and bilirubin periodically. If elevations occur, rifampin should be discontinued, and most animals are expected to recover. Urine will be colored orange to reddish-orange in treated patients. It will also discolor saliva, tears, feces, sclera, and mucous membranes to a reddish-orange color. The discoloration is not pathogenic and is a normal occurrence. Rifampin is unpalatable and may be difficult to administer to some animals. Pancreatitis has been associated with rifampin administration, but not well documented in dogs or cats.

### Contraindications and Precautions

Use cautiously in animals that are at risk for pancreatitis. Because of risk of hepatitis, use cautiously with any other drug that may be potentially hepatotoxic (e.g., sulfonamides, anticonvulsants, acetaminophen). Avoid use in pregnant animals.

### Drug Interactions

Multiple drug interactions are possible. Rifampin is a potent inducer of cytochrome P450 hepatic enzymes. Elevation of cytochrome P450 enzyme activity may persist for 4 days, but returned to baseline by 8 days in people. The duration of this activity is not known in animals. Drugs that may have decreased levels because of rapid metabolism when administered with rifampin include barbiturates, chloramphenicol, progestins, digitalis, warfarin, corticosteroids (prednisolone), and potentially many other drugs concurrently administered with rifampin. Rifampin is also an inducer of membrane efflux pump (P-glycoprotein), which may have the consequence of decreasing oral absorption of other drugs.

## Instructions for Use

Most of the documented clinical experience has been in horses when rifampin was combined with a macrolide antibiotic for use in foals. When selecting a dose, the 10-mg/kg PO dose was adequate for susceptible gram-positive infections in the adult horse. Use in small animals (and doses) is based on experience, primarily in dogs in which rifampin was used to treat methicillin-resistant *Staphylococcus* infections. It is often recommended to administer rifampin in small animals in combination with other drugs to decrease emergence of resistance. However, there is no evidence that this is necessary when treating infections caused by *Staphylococcus* spp., and rifampin may be used as monotherapy in these cases. Administer on an empty stomach whenever possible.

## Patient Monitoring and Laboratory Tests

Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) breakpoint for sensitive organisms is  $\leq 1.0$  mcg/mL. Minimum inhibitory concentrations (MICs) for gram-positive organisms generally occur at 0.1 mcg/mL, whereas

gram-negative organisms have MIC values ranging from 8-32 mcg/mL. Because of the risk of liver injury in dogs, it is advised to periodically (e.g., every 10-14 days) check the liver enzymes and serum bilirubin to monitor for signs of liver injury.

### Formulations

- Rifampin is available in 150-mg and 300-mg capsules and 600-mg Rifadin IV injectable solution.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Rifampin is slightly soluble in water and ethanol. It is more soluble at acidic pH. Acid should be added to solutions (e.g., ascorbic acid) to prevent oxidation and improve solubility. Rifampin has been mixed with syrups and flavorings for oral administration and was stable for 4-6 weeks. The injectable solution is prepared by adding 10 mL of saline to a 600-mg vial and mixing (60 mg/mL). It may be infused with 0.9% saline or 5% dextrose solution. Reconstituted injectable solution is stable for 24 hours.

### Small Animal Dosage

#### Dogs and Cats

- 5 mg/kg q12h PO or 10 mg/kg q24h PO.

### Large Animal Dosage

#### Horses

- 10 mg/kg q24h PO.
- Foals for treatment of *R. equi*: 5 mg/kg q12h PO combined with erythromycin (25 mg/kg q8h PO).

#### Cattle

- 20 mg/kg q24h PO.

### Regulatory Information

Avoid administration in food-producing animals. Withdrawal times have not been established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Ringer's Solution

**Trade and other names:** Generic brands

**Functional classification:** Fluid replacement

### Pharmacology and Mechanism of Action

Intravenous solution for fluid replacement. Ringer's solution contains 147 mEq/L sodium, 4 mEq/L potassium, 155 mEq/L chloride, and 4 mEq/L calcium.

### Indications and Clinical Uses

Ringer's solution is used as a fluid replacement and for maintenance. It has a balanced electrolyte concentration, but it does not contain any bases (see lactated Ringer's for solutions that contain bases).

**Precautionary Information****Adverse Reactions and Side Effects**

Ringer's solution is considered an acidifying solution because with prolonged administration, the chloride will increase renal excretion of bicarbonate. Fluid overload occurs at high infusion rates.

**Contraindications and Precautions**

Do not exceed fluid rates of 80 mL/kg/hr. Consider supplementing with potassium because this fluid will not meet maintenance potassium needs.

**Drug Interactions**

Ringer's solution contains calcium; do not mix with drugs that may bind to calcium.

**Instructions for Use**

When administering IV fluid solution, monitor rate and electrolyte concentrations carefully. Add bicarbonate to fluids, if necessary, based on calculation of base deficit.

Fluid administration rates are as follows: normal maintenance rates: 40-65 mL/kg/24 hr (approximately 2-2.5 mL/kg/hr). For replacement fluid, use the following calculation:

$$\text{Liters needed} = \% \text{ dehydration} \times \text{body weight (kg)}$$

or

$$\text{mL needed} = \% \text{ dehydration} \times \text{body weight (kg)} \times 1000$$

**Patient Monitoring and Laboratory Tests**

Monitor pulmonary pressure when infusing high doses. Monitor electrolyte balance, especially potassium, during treatment.

**Formulations**

Ringer's solution is available in 250-, 500-, and 1000-mL bags for infusion.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats**

- 55-65 mL/kg day (2.5 mL/kg/hr) IV, SQ, or IP (intraperitoneal) for maintenance.
- 15-30 mL/kg/hr IV for moderate dehydration.
- 50 mL/kg/hr IV for severe dehydration.

**Large Animal Dosage****Large Animals**

- 40-50 mL/kg day IV, SQ, or IP for maintenance.
- 15-30 mL/kg/hr IV for moderate dehydration.
- 50 mL/kg/hr IV for severe dehydration.

**Calves**

- Moderate dehydration: 45 mL/kg given at a rate of 30-40 mL/kg/hr.
- Severe dehydration: 80-90 mL/kg given at a rate of 30-40 mL/kg/hr or as fast as 80 mL/kg/hr, if necessary.

**Regulatory Information**

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Robenacoxib

Roe-ben-A-cocks-ib

**Trade and other names:** Onsior (veterinary preparation)

**Functional classification:** Anti-inflammatory

### Pharmacology and Mechanism of Action

Robenacoxib is an NSAID. Like other drugs in this class, robenacoxib has analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. The enzyme inhibited by NSAID is the cyclooxygenase (COX) enzyme. The COX enzyme exists in two isoforms: COX-1 and COX-2. COX-1 is primarily responsible for synthesis of prostaglandins important for maintaining a healthy gastrointestinal tract, kidney function, platelet function, and other normal functions. COX-2 is induced and responsible for synthesizing prostaglandins that are important mediators of pain, inflammation, and fever. However, it is known that there is some crossover of COX-1 and COX-2 effects and COX-2 activity is important for some biological effects. Robenacoxib is more selective for COX-2 using in vitro assays compared with older nonselective NSAIDs, but it is not known if the specificity for COX-1 or COX-2 is associated with efficacy or safety. Robenacoxib has a short half-life in both dogs and cats, but tissue concentrations persist for much longer, which may explain the efficacy with once-daily dosing despite a short half-life. The half-life is 0.6–1.1 hours in dogs and 1.49, 1.87, 0.84, and 0.78 hours in cats (depending on the study). The volume of distribution in dogs is 0.24 L/kg and 0.13 and 0.19 L/kg in cats, depending on the study. Oral absorption is 84% in dogs (nonfed) or 62% (fed) and in cats, 49% (nonfed), and 10% (fed). Protein binding is 98% and 99.9% in dogs and cats, respectively. Thus it appears that feeding greatly influences oral absorption. Therefore, it is recommended in cats that it should be administered without food to maximize oral absorption.

### Indications and Clinical Uses

Robenacoxib is used to decrease pain, inflammation, and fever. The Food and Drug Administration (FDA)-approved dose in cats in the US is 1 mg/kg orally per day for a maximum of 3 days to treat pain associated with surgery and other conditions. It is also approved in Europe for dogs and cats to treat acute pain and inflammation associated with musculoskeletal disorders. Outside the U.S. tablets are approved for treatment of pain and inflammation in dogs associated with chronic osteoarthritis. There is also an injectable solution for treatment of pain and inflammation associated with surgery.

Robenacoxib has not been investigated for use in large animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Major adverse effects are gastrointestinal, including vomiting, diarrhea, and ulceration. In field trials, the most common adverse effects associated with robenacoxib administration were gastrointestinal adverse events (vomiting, soft feces) in cats and dogs; in dogs following long-term oral treatment, an increase in liver enzyme activities may occur, but is not necessarily associated with liver pathology. The solution for injection (not available in the US) might cause pain on injection, presumably because of the excipient in the solution.

Because robenacoxib appears to be relatively COX-2 specific and has a short half-life, adverse effects are expected to be less than other NSAIDs that are not as selective. However, veterinarians should consider the potential for NSAID-induced adverse effects as with any other drug in this class. Kidney injury, especially in dehydrated animals or animals with preexisting renal disease, has been shown for some NSAIDs, including those with COX-2 selectivity.

In safety studies in cats, robenacoxib was well tolerated even when treatment was for longer and at higher doses than approved.

### **Contraindications and Precautions**

Dogs and cats with preexisting gastrointestinal problems or kidney disease may be at a greater risk of adverse effects from NSAIDs. Safety in pregnant animals is not known, but adverse effects have not been reported.

### **Drug Interactions**

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the gastrointestinal adverse effects. Some NSAIDs may interfere with the action of diuretic drugs and ACE inhibitors.

## **Instructions for Use**

The oral tablet may be administered once daily for up to 3 days in the US and for 6 days in Europe. Some cats have received the medication for much longer periods without adverse events. Dogs can be treated for as long as necessary. The suggested dose is 1 mg/kg per day, but the actual dose range is 1-2 mg/kg in dogs or 1-2.4 mg/kg in cats.

In countries where the injection form is available, prior to surgery, administer the injection subcutaneously to cats or dogs approximately 30 minutes before the start of surgery at 2 mg/kg. After surgery it may be continued for an additional 2 days.

The oral absorption is greatly diminished with food in cats, and it is recommended to administer without food or with just one third of the daily ration (small meal).

## **Patient Monitoring and Laboratory Tests**

Monitor gastrointestinal signs for evidence of diarrhea, gastrointestinal bleeding, or ulcers. Because of risk of renal injury, monitor renal parameters (water consumption, blood urea nitrogen [BUN], creatinine, and urine-specific gravity) periodically during treatment. Safety has been evaluated in dogs and cats prior to approval in the respective countries. In safety studies, young healthy cats have tolerated 10 mg/kg q12h for 42 days.

## **Formulations**

- Availability of dose forms among countries can vary. In the US, there are only tablets for cats. In the European countries, there are 6-mg tablets for cats; 5-, 10-, 20-, and 40-mg tablets for dogs; and a 20-mg/mL injectable solution.

## **Stability and Storage**

Store protected from excessive heat and in dry conditions. Stability of compounded formulations has not been evaluated.

## **Small Animal Dosage**

### **Dogs**

- 1-2 mg/kg q24h PO.

### **Cats**

- 1-2.4 mg/kg PO once per day.

## Large Animal Dosage

- No large animal doses have been reported.

## Regulatory Information

Withdrawal times or regulatory information for food-producing animals is not available.

## Romifidine Hydrochloride

roe-mif'ih-deen hye-droe-klor'ide

**Trade and other names:** Sedivet

**Functional classification:** Analgesic,  $\alpha_2$  agonist

## Pharmacology and Mechanism of Action

Alpha<sub>2</sub>-adrenergic agonist. Alpha<sub>2</sub> agonists decrease release of neurotransmitters from the neuron. The proposed mechanism whereby they decrease transmission is via binding to presynaptic alpha<sub>2</sub>-receptors (negative feedback receptors). The result is decreased sympathetic outflow, analgesia, sedation, and anesthesia. Romifidine is structurally similar to clonidine. Other drugs in this class include xylazine, detomidine, dexmedetomidine, and medetomidine. Medetomidine, dexmedetomidine, romifidine, and detomidine are more specific for the alpha<sub>2</sub>-receptor than xylazine. Romifidine has been studied in horses more than other animals. In horses, at 80 mcg/kg, it has a half-life of 2.3 hours and high clearance of 25-38 mL/kg/min.

Romifidine has an onset of effect of 2 minutes and a duration of 1-1.5 hours.

## Indications and Clinical Uses

Romifidine, like other alpha<sub>2</sub>-agonists, is used as a sedative, anesthetic adjunct, and for analgesia. It produces the longest duration of sedative effects, followed by detomidine, medetomidine, and xylazine. A dose of 80 mcg/kg of romifidine IV is equipotent to 1 mg/kg xylazine IV and 20 mcg/kg detomidine IV. Its use is primarily limited to horses in which it is used as a sedative and analgesic to facilitate handling, clinical examinations, clinical procedures, and minor surgical procedures and for use as a preanesthetic prior to the induction of general anesthesia.

## Precautionary Information

### Adverse Reactions and Side Effects

Romifidine, like other alpha<sub>2</sub>-agonists, decreases sympathetic output. Bradycardia is common, and cardiovascular depression may occur. Cardiac effects can include sinoatrial block, first-degree and second-degree AV block, bradycardia, and sinus arrhythmia. In horses, it causes effects similar to other alpha<sub>2</sub>-agonists, including ataxia, head drooping, sweating, and bradycardia. Facial edema is common, especially with higher doses. Even at high doses in experimental horses (up to 600 mcg/kg), there were no deaths.

### Contraindications and Precautions

Romifidine, like other alpha<sub>2</sub>-agonists, should be used cautiously in animals with heart disease. Use may be contraindicated in older animals with preexisting cardiac disease. Xylazine causes problems in pregnant animals, and this also should be considered for other alpha<sub>2</sub>-agonists. Use cautiously in animals that are pregnant; it may induce labor. In addition, it may decrease oxygen delivery to the fetus in late gestation. In case of overdose, reverse with atipamezole or yohimbine.

**Drug Interactions**

Do not use with other drugs that may cause cardiac depression. It may be used in horses with diazepam or ketamine. Do not mix in vial or syringe with other anesthetics. Use with opioid analgesic drugs will greatly enhance the CNS depression. Consider lowering doses if administered with opioids.

**Instructions for Use**

Romifidine, like other  $\alpha_2$ -agonists, can be administered with ketamine or benzodiazepines. It can be reversed with  $\alpha_2$ -antagonists such as atipamezole or yohimbine. A range of doses is used in horses for romifidine; 40 and 120 mcg/kg IV have been compared (80 mcg/kg is a common dose), which showed that sedation, cardiac effects, and analgesia are all dose-dependent effects. At a dose of 80 mcg/kg, strong sedation in horses lasts for approximately 45-60 minutes. Deeper sedation occurs with higher doses. Each dose produced effects for at least 60 minutes, and some were observed for 180 minutes. Duration of 180 minutes is more likely with higher doses.

**Patient Monitoring and Laboratory Tests**

Monitor vital signs during anesthesia. Monitor heart rate, blood pressure, and ECG if possible during anesthesia.

**Formulations**

- Romifidine is available in a 1% injection (10 mg/mL).

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats**

- Doses not established for small animals.

**Large Animal Dosage****Horses**

- Sedation and analgesia: 40-120 mcg/kg IV.
- Preanesthetic: 100 mcg/kg IV.

**Regulatory Information**

Do not administer in animals intended for food.

**Ronidazole**

roe'nid'ah-zole

**Trade and other names:** Generic

**Functional classification:** Antibacterial, antiparasitic

**Pharmacology and Mechanism of Action**

Antibacterial and antiprotozoal drug. It is a nitroimidazole in which the activity involves generation of free nitroradicals via metabolism within protozoa and bacteria. Ronidazole disrupts DNA in an organism via reaction with intracellular metabolites. Its action is specific for anaerobic bacteria and protozoa. Like other nitroimidazoles,

it is active against some protozoa, including *Trichomonas* and *Giardia* and intestinal protozoal parasites. After oral administration in cats, it was rapidly and completely absorbed. The half-life in cats is approximately 10 hours.

### Indications and Clinical Uses

Ronidazole is currently not an FDA-approved drug, but it has been used in cats to treat intestinal protozoal parasites. Studies for treatment of other organisms are not available. For treatment of feline *Tritrichomonas foetus* intestinal infections, it has been administered orally at a dose of 30 mg/kg twice daily for 2 weeks. However, twice-daily administration is more likely to produce CNS reactions, and pharmacokinetic data indicate that 30 mg/kg once daily may be equally effective. Efficacy for long-term remission has not been established, but temporary resolution of feline *T. foetus* intestinal infections has been observed.

### Precautionary Information

#### Adverse Reactions and Side Effects

Like other nitroimidazoles, the most severe adverse effect is caused by toxicity to the CNS. High doses may cause lethargy, CNS depression, ataxia, tremors, hyperesthesia, seizures, vomiting, and weakness. The CNS signs are related to inhibition of action of gamma aminobutyric acid (GABA) and are responsive to benzodiazepines (diazepam). Adverse CNS effects are dose related. Dogs show neurotoxicity at doses of 50–200 mg/kg (seizures, tremors, ataxia). Avoid doses that exceed 60 mg/kg per day in cats. Like other nitroimidazoles, it has the potential to produce mutagenic changes in cells, but this has not been demonstrated in vivo. Like other nitroimidazoles, it has a bitter taste and can cause vomiting and anorexia.

#### Contraindications and Precautions

Fetal abnormalities have not been demonstrated in animals with recommended doses, but use cautiously during pregnancy.

#### Drug Interactions

Like other nitroimidazoles, it may potentiate the effects of warfarin and cyclosporine via inhibition of drug metabolism.

### Instructions for Use

Ronidazole is currently not a marketed drug but has been prepared from bulk powder in compounding pharmacies.

### Patient Monitoring and Laboratory Tests

Monitor for neurologic adverse effects.

### Formulations

- No available formulation exists; it is compounded from bulk chemicals. Intravenous formulations have been prepared by dissolving ronidazole pure powder in 5% dextrose in water (D5W) to a concentration of 3.2 mg/mL. This formulation has been safely administered to research animals.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- No dose has been reported.



**Cats**

- 30 mg/kg q24h PO for 2 weeks. Early clinical studies were performed with 30 mg/kg q12h, but twice-daily administration is more likely to produce CNS toxicity, and an interval of q24h may be equally effective.

**Large Animal Dose**

- No doses have been reported for large animals.

**Regulatory Information**

Do not administer to animals that produce food. Administration of nitroimidazoles to animals intended for food is prohibited. Treated cattle must not be slaughtered for food.

## S-Adenosylmethionine (SAME)

ess'ah-den'oh-sill-meh-thye'oh-neen

**Trade and other names:** Denosyl, Denamarin, and SAME

**Functional classification:** Nutritional supplement

### Pharmacology and Mechanism of Action

Nutritional supplement. S-Adenosylmethionine, usually abbreviated as SAME, is found naturally and is formed from methionine and ATP. It has been associated with improvement in acetaminophen-induced hepatotoxicity in humans and has been beneficial for some conditions that affect the liver according to isolated reports in veterinary medicine. It serves as a methyl donor, catalyzed by methyltransferase. It also is a substrate for a transsulfuration reaction in which demethylated SAME is metabolized to glutathione (GSH). Glutathione may conjugate certain drug metabolites to enhance excretion. Cats and dogs have low levels of GSH, and SAME may help restore GSH in animals that have been intoxicated and perhaps in animals that have liver disease. It is a methyl donor for neurotransmitter metabolism in the synthesis and turnover of biogenic monoamines (central nervous system [CNS] neurotransmitters such as serotonin, dopamine, and norepinephrine). In dogs, the half-life after oral administration is approximately 2 hours.

### Indications and Clinical Uses

SAME has been used as a dietary supplement to support patients with hepatic disease. It may help restore hepatic GSH concentrations in deficient animals. It also has been administered to treat liver injury caused by intoxication of acetaminophen and other drugs that produce hepatotoxic oxidative drug injury. Another dietary supplement, silymarin (see monograph for [silymarin](#) in this book), also known as *milk thistle* and *silybin*, has hepatic antioxidant properties and has been combined with SAME for treatment in dogs and cats (Denamarin). Via the effect on neurotransmitter synthesis, SAME has been used to improve cognitive function in dogs. In dogs older than 8 years, SAME (18 mg/kg/day) improved age-related mental impairment compared to placebo. It has been used to treat arthritis in dogs, but no studies have demonstrated effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

It may produce a self-limiting transient gastric upset. No other adverse effects are reported.

#### Contraindications and Precautions

No contraindications are reported for animals.

#### Drug Interactions

Reactions of SAME with tricyclic antidepressants (TCAs) have been reported, although the mechanism is not known. In laboratory animals, administration with clomipramine has caused serotonin syndrome.

### Instructions for Use

SAME is a dietary supplement widely available without a prescription (over-the-counter [OTC]). Potency of formulations may vary. Absorption is decreased when given with a meal. Administer 30 minutes to 1 hour before feeding. To ensure passage into the stomach of cats, administer with water. Coated tablets (such as

Denosyl) protect the active ingredient from moisture during storage and destruction by stomach acid. Do not break tablets or disrupt coating.

### **Patient Monitoring and Laboratory Tests**

Monitor liver enzymes in animals being treated for toxicity.

### **Formulations**

- SAME is widely available OTC in tablets and powder. The brand Denosyl is available in 90-, 225-, and 425-mg tablets. Veterinary formulations (e.g., Denamarin) may also contain silymarin (silybin) and vitamin E.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Do not disrupt coating on tablet.

### **Small Animal Dosage**

#### **Dogs**

- 20 mg/kg per day PO or 90 mg (small dogs), 225 mg (medium dogs), and 425 mg (large dogs).

#### **Cats**

- 90 mg/cat/day PO up to 5 kg body weight.

### **Large Animal Dosage**

- No dose has been reported for large animals.

### **Regulatory Information**

Because of low risk of harmful residues in food animals, no withdrawal time is suggested.

## **Selamectin**

sel-ah-mek'tin

**Trade and other names:** Revolution

**Functional classification:** Antiparasitic

### **Pharmacology and Mechanism of Action**

Antiparasitic. Microfilaricide for heartworm prevention in dogs and cats. Selamectin is a semisynthetic avermectin. Avermectins (ivermectinlike drugs) and milbemycins (milbemycin, doramectin, and moxidectin) are macrocyclic lactones. Avermectins and macrocyclic lactones share similarities, including mechanism of action. These drugs are neurotoxic to parasites by potentiating glutamate-gated chloride ion channels in parasites. Paralysis and death of the parasite are caused by increased permeability to chloride ions and hyperpolarization of nerve cells. These drugs also potentiate other chloride channels, including ones gated by gamma aminobutyric acid (GABA). Mammals ordinarily are not affected because they lack glutamate-gated chloride channels, and there is a lower affinity for other mammalian chloride channels. Because these drugs ordinarily do not penetrate the blood–brain barrier, GABA-gated channels in the CNS of mammals are not affected. After topical application, selamectin has high affinity for sebaceous glands and skin. The terminal half-life of selamectin is 11 days in dogs and 8 days in cats.

## Indications and Clinical Uses

Selamectin is approved for prevention of heartworms; control of fleas, mites, and ticks in dogs; and prevention of heartworms, control of fleas, mites, hookworms, and roundworms in cats. Selamectin also can be used to treat scabies (*Sarcoptes*) and is sometimes preferred over ivermectin.

### Precautionary Information

#### Adverse Reactions and Side Effects

Transient, localized alopecia, with or without inflammation, at or near the site of application was observed in approximately 1% of treated cats. Other adverse effects included nausea, lethargy, salivation, tachypnea, and muscle tremors.

#### Contraindications and Precautions

Do not use in dogs younger than 6 weeks of age. Do not use in cats younger than 8 weeks of age.

#### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

Apply as indicated on product label to skin of dogs and cats.

## Patient Monitoring and Laboratory Tests

Monitor heartworm status in animals.

## Formulations

- Selamectin is available in 60- and 120-mg/mL transdermal solution.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- Heartworm prevention: 6-12 mg/kg applied topically every 30 days.
- Other parasites: The same dose as for heartworm prevention may be applied for treatment and prevention of ear mites and fleas. In cats, the preferred dose is 6 mg/kg every 30 days.
- Sarcoptic mange treatment: 6-12 mg/kg twice 30 days apart. (However, many dermatologists administer it at 2- to 3-week intervals.)

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

## Selegiline Hydrochloride

se-leh'jeh-leen hye-droe-klor'ide

**Trade and other names:** Anipryl (also known as deprenyl and l-deprenyl), Eldepryl (human preparation), and Emsam transdermal patch

**Functional classification:** Dopamine agonist

### Pharmacology and Mechanism of Action

Dopamine agonist. Selegiline has been known by many names. Selegiline hydrochloride is the official United States Pharmacopeia (USP) drug name, but most clinicians know it by the older name, l-deprenyl. (l-deprenyl is distinguished from its stereoisomer d-deprenyl.) A related drug is rasagiline. Selegiline has been used in humans for treatment of Parkinson disease and occasionally for Alzheimer disease with the trade name *Eldepryl*. (Efficacy for Alzheimer disease has not been established.)

The veterinary formulation is approved for treatment of Cushing disease in dogs and canine cognitive dysfunction. The action of selegiline is to inhibit monoamine oxidase (MAO) type B (and other MAOs at higher doses). The proposed mechanism of action is to inhibit the metabolism of dopamine in the CNS. The action for pituitary-dependent hyperadrenocorticism may be through increased dopamine levels in the brain, which decreases ACTH release, resulting in lower cortisol levels. Secondary effects are related to inhibition of the metabolism of phenylethylamine. (Phenylethylamine in laboratory animals produces amphetamine-like effects.) Two active metabolites are l-amphetamine and l-methamphetamine, but it is not known to what extent these contribute to pharmacologic effects. In horses, the metabolism to amphetamine-like metabolites is low.

### Indications and Clinical Uses

In dogs, selegiline is approved to control clinical signs of pituitary-dependent hyperadrenocorticism (PDH) (Cushing disease) and to treat cognitive dysfunction in older dogs. However, the efficacy for Cushing disease may not be as high as for other drugs such as mitotane or trilostane. Selegiline effects may be limited to PDH caused by lesions of the pars intermedia and may not be effective for other forms of PDH (most cases of canine PDH have lesions of the pars distalis). It may improve some clinical signs without lowering cortisol levels in dogs with PDH when administered 1.0 mg/kg once daily. For canine cognitive dysfunction (dementia) in aged dogs, treatment with selegiline inhibits MAO type B and increases dopamine concentrations in the brain, which restores dopamine and balance and may improve cognitive ability. It has been administered to some older cats with age-related behavior problems, but clinical results in cats have not been reported and doses are based on limited anecdotal experiences. It does not appear to produce any clinical effects in horses from oral administration.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are rare in dogs but have included vomiting, diarrhea, and hyperactive and restless behavior. Amphetamine-like signs can be produced in experimental animals. At high doses in dogs, hyperactivity has been observed (doses >3 mg/kg) that included salivation, panting, repetitive movements, decreased weight, and changes in activity level. At doses of 30 mg per horse IV or PO, there were no behavior effects.

Two active metabolites are l-amphetamine and l-methamphetamine. Even though there were increases in amphetamine concentrations in dogs, they were not high enough to produce adverse effects. However, at high doses ( $>3$  mg/kg) it may produce behavioral changes. The l-isomer metabolites are not as active as their d-forms, and studies have not supported a potential for amphetamine-like abuse or dependency from selegiline compared with other amphetamine-like drugs.

### Contraindications and Precautions

Not indicated for adrenal tumors. Use cautiously with other drugs. (See the following list of interactions.)

### Drug Interactions

Do not use with other monoamine oxidase inhibitors (MAOIs). Do not use with TCAs, such as clomipramine and amitriptyline, or with selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine. Do not administer with meperidine, dobutamine, or amitraz. Use cautiously with sympathetic amines, and other drugs that may produce interactions such as linezolid and tramadol. However, one clinical study showed that there were no adverse effects in dogs when selegiline was administered in combination with phenylpropanolamine.

### Instructions for Use

Dose titration to effect. Start with low dose and increase gradually until clinical effect is observed. The transdermal patch for humans has not been evaluated for animals.

### Patient Monitoring and Laboratory Tests

No specific monitoring is required. Serum cortisol testing is not valuable for evaluating efficacy.

### Formulations

- Selegiline is available in 2-, 5-, 10-, 15-, and 30-mg tablets for animals; 5-mg tablets or capsules for humans; and 20-, 30-, and 40-cm<sup>2</sup> transdermal patch (EmSam) for humans.

### Stability and Storage

Stable if stored in manufacturer's original formulation.

### Small Animal Dosage

#### Dogs

- Begin with 1 mg/kg q24h PO. If there is no response within 2 months, increase dose to maximum of 2 mg/kg q24h PO.

#### Cats

- 0.25-0.5 mg/kg q12h PO. In some cats, once-daily treatment may be sufficient.

### Large Animal Dosage

- No dose has been reported for large animals. In preliminary studies in which selegiline was administered at a dose of 30 mg/horse PO or IV, there were no observed effects on behavior or locomotor activity.

### Regulatory Information

Do not administer to animals intended for food.

Racing Commissioners International (RCI) Classification: 2

## Senna

sen'na

**Trade and other names:** Senokot**Functional classification:** Laxative

### Pharmacology and Mechanism of Action

Laxative. Senna acts via local stimulation or via contact with intestinal mucosa.

### Indications and Clinical Uses

Senna is indicated for treatment of constipation.

#### Precautionary Information

##### Adverse Reactions and Side Effects

Adverse effects not reported for animals. However, excessive doses are expected to cause fluid and electrolyte loss.

##### Contraindications and Precautions

Do not administer to animals with gastrointestinal (GI) obstruction. Do not administer to dehydrated animals.

##### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Doses and indications are not well established for veterinary medicine. Use is strictly based on anecdotal experience.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Senna is available in granules in concentrate or syrup.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- Syrup: 5-10 mL/dog/day PO.
- Granules: 1/2 to 1 tsp/dog/day PO.

#### Cats

- Syrup: 5 mL/cat q24h.
- Granules: 1/2 tsp/cat q24h (with food).

### Large Animal Dosage

- No doses have been reported for large animals.

### Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Sevoflurane

see-voe-floo'raane

**Trade and other names:** Ultane

**Functional classification:** Anesthetic

### Pharmacology and Mechanism of Action

Inhalant anesthetic. Like other inhalant anesthetics, the mechanism of action is uncertain. Sevoflurane produces a generalized, reversible depression of the CNS. The inhalant anesthetics vary in their solubility in blood, their potency, and the rate of induction and recovery. Those with low blood/gas partition coefficients are associated with the most rapid rates of induction and recovery. Sevoflurane has a vapor pressure of 160 mm Hg (at 20° C), a blood/gas partition coefficient of 0.65, and a fat/blood coefficient of 48. Sevoflurane is similar to isoflurane in many respects, except that it has lower solubility, resulting in faster induction and recovery times.

### Indications and Clinical Uses

Sevoflurane is used as an inhalant anesthetic. There are not any significant advantages over the use of isoflurane and it is more expensive than isoflurane. It has a minimum alveolar concentration (MAC) value of 2.58%, 2.36%, and 2.31% in cats, dogs, and horses, respectively. Sevoflurane, like other inhalant anesthetics, can be used with preanesthetics, opioids,  $\alpha_2$ -agonists, and tranquilizers.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are related to anesthetic effects (e.g., cardiovascular and respiratory depression). Sevoflurane can produce byproducts of fluoride ions and compound A, which can be toxic to the kidneys.

#### Contraindications and Precautions

Do not use unless there is an adequate facility to monitor patients.

#### Drug Interactions

No drug interactions have been reported for animals.

### Instructions for Use

Use of inhalant anesthetics requires careful monitoring. Dose is determined by depth of anesthesia.

### Patient Monitoring and Laboratory Tests

Carefully monitor patient's heart rate and rhythm and respiratory rate during use.

### Formulations

- Sevoflurane is available in a 100-mL bottle.

### Stability and Storage

Sevoflurane is highly volatile and should only be stored in approved containers.

### Small Animal Dosage

- Induction: 8%; maintenance: 3%-6%.



**Large Animal Dosage****Horses**

- MAC value: 2.31.

**Regulatory Information**

No withdrawal times are established for animals intended for food. Clearance is rapid and short withdrawal times are suggested. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Sildenafil Citrate**

sill-den'-ah-fil

**Trade and other names:** Viagra, Revatio**Functional classification:** Vasodilator**Pharmacology and Mechanism of Action**

Vasodilator. Sildenafil is a vasodilator specific for phosphodiesterase V. Sildenafil and similar drugs act to increase cyclic GMP by inhibiting its breakdown by phosphodiesterase-V (PDE-V). There are two important locations of PDE V: (1) vascular smooth muscle of the lungs, and (2) corpus cavernosum. The second effect produces the desired clinical effects that have caused the popularity in human medicine. The effect on vascular smooth muscle of the lungs produces vasodilation of the pulmonary vascular bed in patients with pulmonary hypertension. Other drugs that have been used for this effect are tadalafil (Cialis) at a dose of 1-2 mg/kg q12h PO in dogs.

**Indications and Clinical Uses**

Sildenafil and related drugs are used in people for treating erectile dysfunction via the effect on the corpus cavernosum. This effect has not been explored in veterinary medicine. The use in veterinary medicine has been limited to the treatment of pulmonary arterial hypertension. In dogs, sildenafil produced improvement in patients with pulmonary hypertension.

**Precautionary Information****Adverse Reactions and Side Effects**

Cutaneous flushing of the inguinal area has been observed in dogs. Otherwise, adverse effects have not been reported with clinical use in dogs. Potential effects are attributed to the vasodilator action. If high doses or other vasodilators are administered—especially those that increase cyclic-GMP levels—hypotension can occur.

**Contraindications and Precautions**

Use cautiously in conjunction with other vasodilator drugs.

**Drug Interactions**

No drug interactions reported for animals, but in people there are precautions about use with other vasodilators such as alpha blockers and nitrates.

**Instructions for Use**

The use in veterinary medicine has been based on studies in dogs with pulmonary hypertension. The dosages and clinical use are based on these limited reports.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary, but monitor the patient's cardiovascular function (blood pressure and heart rate) in animals at risk for cardiovascular complications.

## Formulations

- Sildenafil is available as 20-, 25-, 50-, and 100-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 2 mg/kg q12h PO. Dose interval may range from 8-24 hours, and doses as high as 3 mg/kg have been administered to some dogs.

### Cats

- 1 mg/kg q8h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No withdrawal times are established for animals intended for food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Silymarin

sill-ih-mare'in

**Trade and other names:** Silybin, Marin, milk thistle, and generic brands

**Functional classification:** Hepatic protectant

## Pharmacology and Mechanism of Action

Silymarin contains silybin as the most active ingredient. It is also known as milk thistle, from which it is derived. Silymarin is a mixture of antihepatotoxic flavonolignans (derived from the plant *silybum*). Silymarin has three components that are considered flavonolignans: silidianin, silcristin, and silybin (which is the major component and also called *silymarin* and *silibinin*). Silymarin has been used for the treatment of a variety of liver disorders in humans. The mechanism of silymarin's action is thought to be as an antioxidant inhibiting both peroxidation of lipid membranes and glutathione oxidation. Experimental data have supported the hepatoprotective properties of silymarin as an antioxidant and a free radical scavenger.

There are limited pharmacokinetic studies in animals. One product (Marin) is complexed with phosphatidylcholine, which may increase bioavailability. The combination products contain vitamin E (aqueous alpha tocopherol, 10-100 IU/kg/day), which has also been advocated for its antioxidant effects.

The pharmacokinetics of silymarin have been studied in dogs, cats, and horses. After oral administration to cats, the half-life is 3.2 hours ( $\pm 1.74$ ) and the oral absorption is low (e.g., 7% in cats). However, the bile concentrations are much higher than serum levels, which may indicate that higher levels occur in the liver. In horses, the oral absorption is extremely low (0.6%) when administered in feed and 2.9% when administered with a nasogastric tube.

## Indications and Clinical Uses

Silymarin has been used to treat hepatic disease, including hepatotoxic reactions in people and animals. It has been administered to animals for the hepatoprotective effects after hepatotoxic drug injury caused by carbon tetrachloride, mushrooms, arsenic, and acetaminophen. It has also been recommended for dogs, cats, and horses with liver disease, but there are no well-controlled clinical studies documenting effectiveness for this use. In one study, the combination product with silymarin and SAME reduced liver enzyme elevations associated with chemotherapy in tumor-bearing dogs. Studies in humans produced mixed results, and studies in dogs, cats, and horses are limited.

In cats, it may provide antioxidant activity. Silymarin is used as a complementary treatment in canine and feline liver disease. However, there is no specific information on the oral absorption, correct dose, or evidence of efficacy of silymarin treatment. Silymarin can be used with S-adenosylmethionine (SAME). There are preparations that include both silymarin and SAME (Denamarin).

When administered to horses, it produced only minor changes in antioxidant capacity of blood.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse reactions have been reported.

#### Contraindications and Precautions

No contraindications have been reported for animals.

#### Drug Interactions

No drug interactions have been reported.

## Instructions for Use

SAME, silymarin, and vitamin E are considered dietary supplements and, as such, are not subject to regulation as drugs by the FDA. Products available OTC and through various outlets may differ considerably in purity and potency.

## Patient Monitoring and Laboratory Tests

Monitor liver enzymes in animals being treated for toxicity.

## Formulations

- Silymarin tablets are widely available OTC. Commercial veterinary formulations (Marin) also contain zinc and vitamin E in a phosphatidylcholine complex in tablets for dogs and cats. The combination of Denamarin contains both silymarin and SAME.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- 5-15 mg/kg PO once daily. Some sources recommend a higher dose of a minimum of 30 mg/kg PO per day.

## Large Animal Dosage

### Horses

- No clinically effective doses have been reported for large animals. At doses of 6.5, 13, and 26 mg/kg q12h for 7 days, only minor antioxidant effects were observed.

## Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Sodium Bicarbonate

**Trade and other names:** Baking soda, soda mint, Citrocarbonate, and Arm & Hammer pure baking soda

**Functional classification:** Alkalinizing agent

## Pharmacology and Mechanism of Action

Alkalinizing agent. Antacid. It increases plasma and urinary concentrations of bicarbonate. One gram sodium bicarbonate is equal to 12 mEq sodium and bicarbonate ions; 3.65 g sodium bicarbonate is equal to 1 g sodium.

## Indications and Clinical Uses

Sodium bicarbonate is a typical alkalinizing solution. It is the most frequent alkalinizing solution used for IV therapy of systemic acidosis and to treat severe hyperkalemia. When adding to fluid therapy, the goal is to maintain PaCO<sub>2</sub> within 37-43 mm Hg. It also has been administered to alkalinize urine.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects have been attributed to alkalinizing activity. Hypokalemia may occur with excessive administration. Hyperosmolality, hyponatremia, paradoxical CNS, and intracellular acidosis may occur.

### Contraindications and Precautions

Do not administer to animals with hypocalcemia (may exacerbate tetany). Do not administer to animals with excessive chloride loss because of vomiting. Do not administer to animals with alkalosis. Administration of sodium bicarbonate may increase risk of hyponatremia, paradoxical CNS acidosis, and hyperosmolality.

### Drug Interactions

Sodium bicarbonate should not be mixed with drugs that require an acidic medium for stability and solubility. Such drugs may include solutions containing hydrochloride (HCl) salts. When mixing IV solutions, do not mix bicarbonate with solutions containing calcium (chelation may result). When administered orally, interaction may occur to decrease absorption of other drugs (partial list includes anticholinergic drugs, ketoconazole, fluoroquinolones, and tetracyclines).

## Instructions for Use

When used for systemic acidosis, doses should be adjusted on the basis of blood gas measurements or assessment of acidosis. The following equation may be used to estimate requirement:

$$\text{mEq Bicarbonate needed} = \text{body weight (kg)} \times \text{base deficit (mEq/L)} \times 0.3.$$

Initially, administer 25%-50% of this dose in IV fluids over 20-30 minutes. In calves or neonates, use a factor of 0.5 instead of 0.3. Note: 1.4% solution = 0.17 mEq/mL and provides 13 g of bicarbonate per L. 8.5 % solution = 1 mEq/mL

## 730 Sodium Chloride 0.9%

of  $\text{NaHCO}_3$ . One teaspoon of baking soda is approximately 2 g of  $\text{NaHCO}_3$ . 12 mEq of bicarbonate is equivalent to 1 g of sodium bicarbonate. When used during cardiac resuscitation, caution is advised because of risk of hyperosmolality, hypernatremia, and paradoxical CNS acidosis.

### Patient Monitoring and Laboratory Tests

Monitor acid–base status.

### Formulations

- Sodium bicarbonate is available in 325-, 520-, and 650-mg tablets. Per teaspoonful (3.9 g) of Citrocarbonate, there is 780 mg sodium bicarbonate and 1.82 grams sodium citrate. It is also available in injections of various strengths: 4.2% is 0.5 mEq/mL (11.5 mg/mL sodium) and 8.4% is 1 mEq/mL (23 mg/mL sodium).

### Stability and Storage

Store in a tightly sealed container at room temperature. Alkaline solution with pH of 7–8.5. Do not mix with acid solutions. Sodium bicarbonate is soluble in water. If exposed to air, it may decompose to sodium carbonate, which is more alkaline.

### Small Animal Dosage

#### Dogs and Cats

- Metabolic acidosis: 0.5–1 mEq/kg IV.
- Renal failure: 10 mg/kg q8–12h PO.
- Alkalinization of urine: 50 mg/kg q8–12h PO.
- Antacid: 2–5 g mixed with water PO.
- CPR: 1 mEq/kg with additional doses of 0.5 mEq/kg at 10-minute intervals.

### Large Animal Dosage

- Metabolic acidosis: 0.5–1 mEq/kg IV slowly. Other doses should be calculated based on base deficits. Oral doses vary. 10–12 grams of sodium bicarbonate may be given orally to adult large animals (horses and cattle) and 2–5 grams to calves, foals, and pigs.

### Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Sodium Chloride 0.9%

**Trade and other names:** Normal saline and generic brands

**Functional classification:** Fluid replacement

### Pharmacology and Mechanism of Action

Sodium chloride is used for IV infusion as replacement fluid. It is not a suitable maintenance solution. Sodium chloride (0.9%) contains 154 mEq/L sodium and 154 mEq/L chloride. See Appendix L for comparison to other fluid solutions.

### Indications and Clinical Uses

Sodium chloride is used for IV fluid supplementation. However, it is not a balanced electrolyte solution and should not be used for maintenance. It also is frequently used as a vehicle to deliver IV medications via constant-rate infusion (CRI).

## Precautionary Information

### Adverse Reactions and Side Effects

It is not a balanced electrolyte solution. Long-term infusion may cause electrolyte imbalance. Saline solution is not balanced, and it may cause acidemia because it will increase renal elimination of bicarbonate. Prolonged use may cause hypokalemia.

### Contraindications and Precautions

Do not exceed maximum dose rate of 80 mL/kg/hr. This solution does not contain electrolyte balance for maintenance.

### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

When administering IV fluid solution, monitor rate and electrolyte concentrations carefully.

Fluid administration rates are as follows:

Replacement fluid: calculate as liters needed = % dehydration  $\times$  body weight (kg)

or

Milliliters needed = % dehydration  $\times$  body weight (kg)  $\times$  1000.

Add bicarbonate to fluids if necessary based on calculation of base deficit.

## Patient Monitoring and Laboratory Tests

Monitor hydration status and serum electrolytes, particularly potassium.

## Formulations

- Sodium chloride 0.9% is available in a 500- and 1000-mL infusion.

## Stability and Storage

Store in a tightly sealed container at room temperature.

## Small Animal Dosage

### Dogs and Cats

- Maintenance administration (no deficits): 1.5-2.5 mL/kg/hr (caution: this is not a balanced maintenance solution).
- Moderate dehydration: 15-30 mL/kg/hr IV.
- Severe dehydration: 50 mL/kg/hr IV.

## Large Animal Dosage

- 40-50 mL/kg day IV, IP, or SQ maintenance.
- Moderate dehydration: 15-30 mL/kg/hr IV.
- Severe dehydration: 50 mL/kg/hr IV.

### Calves

- Moderate dehydration: 45 mL/kg given at a rate of 30-40 mL/kg/hr.
- Severe dehydration: 80-90 mL/kg given at a rate of 30-40 mL/kg/hr or as fast as 80 mL/kg/hr if necessary.

## Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Sodium Chloride 7.2%

**Trade and other names:** Hypertonic saline solution and HSS

**Functional classification:** Fluid replacement

### Pharmacology and Mechanism of Action

Concentrated sodium chloride used for acute treatment of hypovolemia. Hypertonic saline solution causes rapid expansion of plasma volume and may improve microvascular blood flow. Hypertonic saline solution contains 2566 mOsm/L, 1232 mEq/L sodium, and 1232 mEq/L chloride.

### Indications and Clinical Uses

Hypertonic saline is used to treat hypovolemic shock in animals. The duration of its benefit is short lived. There may be benefits for combination with colloids such as Dextran 70. It has been used at doses of 4 mL/kg IV to dogs during a 5-minute infusion to be effective for treatment of septic shock.

### Precautionary Information

#### Adverse Reactions and Side Effects

This is not a balanced electrolyte solution. Long-term infusion may cause electrolyte imbalance.

#### Contraindications and Precautions

Do not administer to hypernatremic animals. Do not administer solutions high in sodium to animals with renal insufficiency.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Hypertonic saline is used for short-term infusion for rapid replacement of vascular volume.

### Patient Monitoring and Laboratory Tests

Monitor hematocrit and blood pressure in treated animals.

### Formulations

- Sodium chloride 7.2% is available as an infusion.

### Stability and Storage

Store in a tightly sealed container at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 3-8 mL/kg IV of 7.2% solution. (Rate of administration should not exceed 1 mL/kg/min.)

### Large Animal Dosage

- 4-8 mL/kg of 7.2% solution IV at a rate of 1 mL/kg/min.

### Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Sodium Iodide (20%)

**Trade and other names:** Iodopen and generic brands

**Functional classification:** Iodine replacement

### Pharmacology and Mechanism of Action

Sodium iodide is used to treat iodine deficiency.

### Indications and Clinical Uses

Sodium iodide is used to treat fungal infections and is preferred over potassium iodide. It has been used for bacterial, actinomycete, and fungal infections, primarily in horses and cattle. In cattle, it has been used for actinomycosis (lumpy jaw) and actinobacillosis (wooden tongue and necrotic stomatitis). In small animals, it has been used for sporotrichosis. Proof of efficacy for these indications has not been established. See monographs on iodide (EDDI) and potassium iodide for additional information on use and formulations available.

### Precautionary Information

#### Adverse Reactions and Side Effects

High doses can produce signs of iodism, which include lacrimation, irritation of mucous membranes, swelling of eyelids, cough, dry and scruffy coat, and hair loss. Potassium iodide has a bitter taste and can cause nausea and salivation.

#### Contraindications and Precautions

Do not use in pregnant animals; it may cause abortion.

#### Drug Interactions

No drug interactions have been reported.

### Instructions for Use

For treatment in cattle, administer slowly by IV. Be careful not to inject outside the vein or tissue necrosis may occur. Clinical use in animals is primarily empirical. The doses and indications listed have not been tested in clinical trials. Other, more proven drugs for these indications should be considered as alternatives.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Sodium iodide is available in a 20-g/100 mL (20%) injection, and there is 100-mcg elemental iodide (118 mcg sodium iodide) per mL injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- Consult oral dose for potassium iodide.

### Large Animal Dosage

#### Horses

- 125 mL of a 20% solution IV daily for 3 days, then 30 g/horse daily injection for 30 days.



## 734 Sotalol Hydrochloride

### Cattle

- 67 mg/kg IV (15 mL per 100 pounds) slowly, and repeat weekly.

### Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Sotalol Hydrochloride

soe'tah-lole hye-droe-klor'ide

**Trade and other names:** Betapace

**Functional classification:** Beta blocker, antiarrhythmic

### Pharmacology and Mechanism of Action

Non-specific beta-receptor ( $\beta_1$  and  $\beta_2$ ) adrenergic blocker (Class II antiarrhythmic). Action is similar to propranolol (one-third potency); however, its beneficial effect may be caused more by the other antiarrhythmic effects. In addition to being a Class II antiarrhythmic drug, sotalol may have some Class III (potassium-channel-blocking) activity. The Class III activity prolongs the refractory period by decreasing potassium conduction in delayed rectifier currents. Sotalol is a water-soluble beta blocker and relies less on the liver for clearance than other beta blockers. Plasma levels and interindividual differences in clearance are expected to be less than other beta blockers.

### Indications and Clinical Uses

Sotalol is indicated for control of refractory ventricular arrhythmias. It has also been used for refractory atrial fibrillation. Although sotalol is commonly administered to small animals, particularly dogs, the use and doses are derived primarily from anecdotal and clinical experience.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported for animals but are expected to be similar to propranolol. Like many antiarrhythmic agents, sotalol may have some proarrhythmic activity. Negative inotropic effects may cause concern in some animals with poor cardiac contractility.

#### Contraindications and Precautions

Administer cautiously to patients with heart failure or AV block. Use cautiously in patients with poor cardiac reserve.

#### Drug Interactions

Use cautiously with other drugs that may decrease cardiac contractility or lower heart rate.

### Instructions for Use

The beta-blocking effects occur at low doses; Class III antiarrhythmic effects occur at higher doses. In people, it may be a more effective maintenance agent for controlling arrhythmias than other drugs.

## Patient Monitoring and Laboratory Tests

Monitor heart rate during treatment.

## Formulations

- Sotalol is available in 80-, 120-, 160-, and 240-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Sotalol is soluble in both water and ethanol. It has been mixed with syrups and flavorings and is stable for 12 weeks, but it should be stored in the refrigerator.

## Small Animal Dosage

### Dogs

- 1-2 mg/kg q12h PO. (For medium- to large-breed dogs, begin with 40 mg/dog q12h, then increase to 80 mg if no response.)

### Cats

- 1-2 mg/kg q12h PO. A dose of 10-20 mg per cat q12h also has been used.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 3

## Spectinomycin, Spectinomycin Dihydrochloride Pentahydrate

spek-tih-noe-mye'sin

**Trade and other names:** Spectam, Spectogard, Prospec, and Adspect

**Functional classification:** Antibiotic, aminocyclitol

## Pharmacology and Mechanism of Action

Spectinomycin is an aminocyclitol antibiotic, which shares similar features with an aminoglycoside. However, it differs in that it does not contain amino sugars or glycosidic bonds. It has a broad spectrum of activity. It is highly water soluble and is easily mixed in aqueous solutions. Spectinomycin, like aminoglycosides, inhibits protein synthesis via a 30S ribosomal target. It is a broad-spectrum drug with activity against gram-positive and some gram-negative bacteria and *Mycoplasma*, but little anaerobic activity. It is not absorbed orally but is administered either in drinking water for treatment of enteritis or by injection for other infections. After injection, the half-life in animals is 1-2 hours.

## Indications and Clinical Uses

Spectinomycin has in vitro activity against some gram-negative bacteria and has also been administered orally for treatment of bacteria enteritis caused by *Escherichia coli* and as an injection for treatment of respiratory infections. Spectinomycin has been used in cattle to treat respiratory infections caused by *Pasteurella*, *Mannheimia*, and *Histophilus somni* (formerly *Haemophilus somnus*). It also has activity against

## 736 Spectinomycin, Spectinomycin Dihydrochloride Pentahydrate

*Mycoplasma*. It has been used in dogs but not commonly. Spectinomycin has been withdrawn by the original drug sponsor and may not be commercially available.

### Precautionary Information

#### Adverse Reactions and Side Effects

Injection site lesions may occur from administration to cattle.

#### Contraindications and Precautions

The powder intended to be used in drinking water should not be formulated with water or saline for IV injection. This solution has produced severe pulmonary edema and death.

#### Drug Interactions

No drug interactions are reported.

### Instructions for Use

Injections in cattle should be made in the neck muscle.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Spectinomycin is available in an oral solution, powder for drinking water, and injection for cattle. Spectinomycin injectable was discontinued by the drug sponsor and may not be available. It was previously available in a 100-mg spectinomycin sulfate/mL solution (Adspec). The lincomycin-spectinomycin combination contains 50 mg lincomycin with 100 mg spectinomycin ("Linco-Spectam") per milliliter. Formulations for poultry include 500 mg per gram water-soluble powder.

### Stability and Storage

Store at room temperature. Protect from freezing. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 22 mg/kg q12h PO for 4 days.
- 5.5-11 mg/kg q12h IM for 4 days.

### Large Animal Dosage

#### Pigs

- 6.6-22 mg/kg q12-24h IM or 50-100 mg/pig PO.

#### Cattle

- 10-15 mg/kg q24h SQ (in neck) for 3-5 days.

### Regulatory Information

Cattle withdrawal time for meat: 11 days. Discoloration of meat at site of injection may persist for 15 days.

Pig withdrawal time for meat: 21 days. At doses of 20 mg/kg, the withdrawal time is 30 days.

Do not administer to calves to be slaughtered for veal. A milk discard time has not been established. Do not administer to dairy cattle 20 months of age or older.

## Spinosad

Spin-oh'-sad

**Trade and other names:** Comfortis and Trifexis (with milbemycin)

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Spinosad is a member of the spinosyns class of insecticides. These resemble tetracycline macrolides but are not antibacterial. Spinosad is a combination of spinosyn A and spinosyn D, derived from bacteria (*Saccharopolyspora spinosa*). The action of spinosad in fleas is activation of nicotinic acetylcholine receptors but not other nicotinic receptors or GABA receptors. The actions in insects treated with spinosad are muscle contractions and tremors in motor neurons, paralysis, and flea death. It does not affect mammals because of differences in the susceptibility of nicotinic acetylcholine receptors.

### Indications and Clinical Uses

Spinosad is used as a monthly treatment for flea infestations. After administration, spinosad can kill fleas within 30 minutes and has complete kill within 4 hours. Efficacy may decline after the initial 2 weeks of treatment in areas with heavy flea populations, and efficacy for treating fleas may be better if administered every 2 weeks, than once per month in some dogs.

Spinosad plus milbemycin is indicated for prevention of heartworm disease (*Dirofilaria immitis*), as well as for killing fleas (*Ctenocephalides felis*), and the treatment and control of adult hookworm (*Ancylostoma caninum*), adult roundworm (*Toxocara canis* and *Toxascaris leonina*), and adult whipworm (*Trichuris vulpis*) infections in dogs and puppies 8 weeks of age or older and 2.5 kg of body weight or greater.

### Precautionary Information

#### Adverse Reactions and Side Effects

In safety studies, administration of high doses (100 mg/kg once daily for 10 days) did not produce any serious adverse effects other than vomiting and mild elevation of liver enzymes. Oral administration of spinosad (300 mg/kg) to collie dogs with the multidrug resistant (MDR) gene mutation (p-glycoprotein deficient) did not cause signs of toxicosis. Occasional vomiting may be observed with routine use (see “[Instructions for Use](#)” section about dosing after vomiting.)

In cats, the most common adverse event was vomiting.

#### Contraindications and Precautions

It can be used safely with heartworm preventatives, including ivermectin, but do not administer with high-dose ivermectin for treatment of *Demodex*. Use cautiously in pregnant and breeding animals. Some adverse effects on puppies have been reported from safety studies on pregnant dogs. Adverse effects in puppies nursing from dams administered spinosad also have been reported.

#### Drug Interactions

Spinosad significantly increased ivermectin concentrations when both drugs were administered together. The proposed interaction is caused by inhibition of P-glycoprotein membrane transporter, which may increase the risk of adverse effects caused by ivermectin. Spinosad has been used safely with other drugs, including heartworm preventatives.

**Instructions for Use**

Spinosad should be administered with food for maximum absorption. If vomiting occurs within an hour of administration, redose with another full dose. If a dose is missed, administer Comfortis chewable tablets with food and resume a monthly dosing schedule. Treatment with spinosad may begin at any season of the year, preferably started before fleas emerge. It can also be used year-round.

Although not approved for cats in the US (but approved in some countries), spinosad has been used safely with once-monthly treatment to control fleas.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Spinosad is available in five chewable tablet sizes containing 140, 270, 560, 810, or 1620 mg.
- Spinosad + milbemycin chewable tablets are available as 140 mg spinosad and 2.3 mg milbemycin oxime, 270 mg spinosad and 4.5 mg milbemycin oxime, 560 mg spinosad and 9.3 mg milbemycin oxime, 810 mg spinosad and 13.5 mg milbemycin oxime, and 1620 mg spinosad and 27 mg milbemycin oxime.

**Stability and Storage**

Store in blister packs and at room temperature.

**Small Animal Dosage****Dogs**

- 30 mg/kg (13.5 mg/lb) PO administered once per month.

**Cats**

- 50-100 mg/kg PO once per month. (The approved dose in some countries for cats is 50 mg/kg once per month.)

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Spironolactone**

speer-one-oh-lak'tone

**Trade and other names:** Aldactone, Prilactone (Europe)

**Functional classification:** Diuretic

**Pharmacology and Mechanism of Action**

Potassium-sparing diuretic. The action of spironolactone is to interfere with sodium reabsorption in distal renal tubules by competitively inhibiting the action of aldosterone. Aldosterone mediates retention of water and sodium. Spironolactone binds directly to the aldosterone receptor, but at usual doses it does not block the action of other steroid receptors. It is more properly referred to as an *aldosterone antagonist* rather than a diuretic because it does not produce a significant diuretic action.

Because aldosterone may have direct effects on remodeling of cardiac muscle cells and vascular endothelium, spironolactone may act by blunting aldosterone-induced myocardial remodeline and myocardial fibrosis. There are minor antiandrogenic effects produced; therefore, a related drug, eplerenone (Inspra), has been used in people because it produces fewer antiandrogenic effects compared to aldosterone. But the endocrine effects and anti-androgenic effects are not as much of a problem in dogs compared with people, and spironolactone is still the preferred agent in this class.

In dogs, the oral absorption is 50%, but is increased to 80%-90% when administered with food. At the currently recommended dose in dogs (2 mg/kg), it produces approximately 88% inhibition of aldosterone.

### Indications and Clinical Uses

Spironolactone is used for treating high blood pressure and congestion caused by heart failure. It is approved in Europe (Prilactone) for dogs to be used with standard therapy for the treatment of congestive heart failure caused by valvular disease (other treatments can include pimobendan, digoxin, and furosemide). Spironolactone may also be used with angiotensin-converting enzyme (ACE) inhibitors to achieve a synergistic effect for treatment of heart failure in animals. The addition of spironolactone to traditional cardiac therapy significantly reduced risk of cardiac morbidity and mortality in dogs with valvular disease. The proposed benefit of spironolactone treatment is via aldosterone antagonism and can be used to inhibit the renin-angiotensin-aldosterone system (RAAS) activation that occurs from diuretic administration (e.g., furosemide) or with some diseases that produce congestion. Spironolactone has also been used for managing hepatic cirrhosis because it will inhibit ascites formation caused by excess aldosterone. It has not been beneficial for treatment in cats with hypertrophic cardiomyopathy (see also “[Adverse Reactions and Side Effects](#)” section for more information on cats).

### Precautionary Information

#### Adverse Reactions and Side Effects

Spironolactone can produce hyperkalemia in some patients. High doses and long-term use may produce some steroid-like side effects. Facial dermatitis has been reported from administration of spironolactone to cats, which may limit its clinical use in these animals. The mechanism of these reactions is not known. In humans, treatment with spironolactone has been associated with antiandrogenic effects such as gynecomastia, hirsutism, and impotence. Antiandrogenic effects have not been reported from its use in animals, except that prostatic atrophy has been observed in some male dogs.

#### Contraindications and Precautions

Do not use in patients that are dehydrated. Nonsteroidal anti-inflammatory drugs (NSAIDs) may interfere with action. Avoid concurrent use of supplements that are high in potassium. Do not administer to patients with gastric ulcers or who may be prone to GI disease such as gastritis or diarrhea.

#### Drug Interactions

Spironolactone is often used together with ACE inhibitors, such as enalapril. It acts synergistically with ACE inhibitors and does not ordinarily produce adverse changes in potassium concentrations. However, in some animals, the dual treatment with spironolactone and an ACE inhibitor may increase risk of kidney injury and may increase risk of hyperkalemia, and some monitoring is advised.

Use cautiously with other drugs that can increase potassium concentrations such as trimethoprim and NSAIDs. Other cardiac treatments have been safely administered with spironolactone such as pimobendan, digoxin, and furosemide.

### Instructions for Use

Spironolactone usually is administered with other drugs (e.g., ACE inhibitors, inotropic agents, vasodilators) for treating congestive heart failure.

### Patient Monitoring and Laboratory Tests

Monitor serum potassium concentration when administering with an ACE inhibitor (e.g., enalapril maleate). Administration of spironolactone may cause a slightly false-positive result for digoxin assay.

### Formulations

- Spironolactone is available in 25-, 50-, and 100-mg tablets. Tablets can be split easily. In Europe there is an approved formulation for animals. In the United States, the human generic formulation is used.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Spironolactone is insoluble in water, but it is slightly more soluble in ethanol. It has been mixed with syrups for an oral suspension (after first mixing with ethanol) and found to be stable for 90-160 days.

### Small Animal Dosage

#### Dogs

- 2-4 mg/kg/day (or 1-2 mg/kg q12h) PO. In dogs, start with 2 mg/kg/day and increase gradually, not to exceed 4 mg/kg/day. In Europe, the approved dose for dogs is 2 mg/kg per day.

#### Cats

- Use in cats is controversial because it may produce dermatitis and because the efficacy is questionable. However, doses in the range of 2-4 mg/kg/day (or 1-2 mg/kg q12h) PO have been administered for some conditions.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use with withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723). RCI Classification: 4

## Stanozolol

stan-oh'zoe-lole

**Trade and other names:** Winstrol-V

**Functional classification:** Hormone, anabolic agent

## Pharmacology and Mechanism of Action

Anabolic steroid. Stanozolol is a derivative of testosterone. Anabolic agents are designed to maximize anabolic effects while minimizing androgenic action. Other anabolic agents include boldenone, nandrolone, oxymetholone, and methyltestosterone.

## Indications and Clinical Uses

Anabolic agents, such as stanozolol, have been used for reversing catabolic conditions, increasing weight gain, increasing muscling in animals, and stimulating erythropoiesis. It has been used in horses during training. Stanozolol has been used in animals with chronic kidney disease and there is some evidence of an improvement in the nitrogen balance in dogs with renal disease treated with stanozolol. Use in cats is associated with toxicity.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects from anabolic steroids can be attributed to the pharmacologic action of these steroids. Increased masculine effects are common. Increased incidence of some tumors has been reported in people. Some 17-alpha-methylated oral anabolic steroids (oxymetholone, stanozolol, and oxandrolone) are associated with hepatic toxicity. Stanozolol administration in cats with kidney disease has been shown to consistently produce increased hepatic enzymes and hepatic toxicosis.

#### Contraindications and Precautions

Do not administer to cats with kidney disease. Use cautiously in dogs that have other preexisting disease such as liver failure. Do not administer to pregnant animals. Stanozolol, like other anabolic steroids, has a high potential for abuse in humans. This drug is abused by humans to enhance athletic performance.

#### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

For many indications, use in animals (and doses) is based on experience in people or anecdotal experience in animals.

## Patient Monitoring and Laboratory Tests

Monitor liver enzymes for signs of hepatic injury (cholestatic) during treatment.

## Formulations

- Stanozolol is available in a 50-mg/mL injection as a sterile suspension and 2-mg tablets. However, there has been limited availability of veterinary injectable formulations. Commercial forms have been withdrawn from the market, but some compounding sources still persist.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 2 mg/dog (or range of 1-4 mg/dog) q12h PO.
- 25-50 mg/dog/week IM.



**Cats**

- 1 mg/cat q12h PO.
- 25 mg/cat/week IM (use cautiously in cats).

**Large Animal Dosage****Horses**

- 0.55 mg/kg (5 mL per 1000 pounds) IM once a week for up to 4 weeks.

**Regulatory Information**

Stanozolol is a Schedule III controlled drug and should not be administered to animals that produce food.

RCI Classification: 4

**Streptozocin**

strep-toe-zoe'sin

**Trade and other names:** Streptozotocin and Zanosar

**Functional classification:** Antihyperglycemic agent

**Pharmacology and Mechanism of Action**

Streptozocin (also known as streptozotocin) is an agent with specific effects on pancreatic beta cells. Because pancreatic beta cells have high concentrations of glucose transporter 2 (GLUT2), streptozocin is selectively toxic to these cells. It is a nitrosourea alkylating agent with selective uptake into pancreatic beta cells because of similarity to glucose in structure. It can produce diabetes mellitus in normal animals, but it is used primarily for treating insuloma tumors in animals. Occasionally it has been used as a cytotoxic agent for treating other tumors in humans (e.g., lymphoma, sarcomas), but these uses are not reported for animals. Streptozocin has a rapid half-life in animals, but metabolites may be active.

**Indications and Clinical Uses**

In animals, streptozocin is used primarily for treating insulin-secreting tumors (insulinoma). It has been used in experimental animals to create models of diabetes mellitus.

**Precautionary Information****Adverse Reactions and Side Effects**

Diabetes mellitus is anticipated in treated animals. In humans, the major adverse effect is kidney injury caused by tubular necrosis. Kidney injury has been reported in dogs at doses greater than 700 mg/m<sup>2</sup>. Other adverse effects include vomiting, nausea, and diarrhea. The gastrointestinal toxicity occurs immediately or within 4 hours of administration, but usually resolves within 24 hours. Increases in hepatic enzymes and hepatic injury have been reported in dogs; however, hepatotoxicity appears to be reversible. Bone marrow suppression is rare in animals. Local phlebitis may occur from IV administration.

**Contraindications and Precautions**

Streptozocin may produce diabetes mellitus in treated animals. In addition, there may be a sudden release of insulin after IV administration, and IV dextrose should

be available to treat acute hypoglycemia. Monitor animals for evidence of renal and hepatic injury. Do not administer to pregnant animals.

### Drug Interactions

No specific drug interactions are reported for animals; however, use with any other nephrotoxic, hepatotoxic, or myelotoxic drug will exacerbate toxicity.

### Instructions for Use

Risk of renal toxicosis caused by streptozocin may be decreased with administration of fluid diuresis. The diuresis should consist of administration of fluids (e.g., 0.9% saline) intravenously prior to drug administration. Antiemetics should be administered with each infusion because vomiting is common. Treatment is continued every 3 weeks until signs of tumor recurrence occur or until toxicosis limits the continuation of treatments. Reconstitute vial prior to use by adding 9.5 mL of 5% dextrose or 0.9% saline to vial. Resulting solution is 100 mg per mL. Further dilute this vial with 5% dextrose or 0.9% saline for IV infusion.

### Patient Monitoring and Laboratory Tests

Monitor serum glucose in treated animals. Monitor serum creatinine, urea nitrogen, and hepatic enzymes for evidence of hepatotoxicity and renal injury. Although myelotoxicity is unusual, monitor complete blood count (CBC) before each treatment.

### Formulations

- Streptozocin is available in 1-g vials for injection.

### Stability and Storage

Store vial between 2° C and 8° C. Use vial within 12 hours after reconstitution at room temperature. Formulation also contains citric acid. Do not use if color changes from pale yellow to a darker brown because this indicates degradation.

### Small Animal Dosage

#### Dogs

- 500 mg/m<sup>2</sup> IV infused over 2 hours every 3 weeks (use with a saline diuresis).

#### Cats

- A safe dose has not been reported for cats.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Do not administer to animals that produce food.

## Succimer

suks'ih-mer

**Trade and other names:** Chemet

**Functional classification:** Antidote

## Pharmacology and Mechanism of Action

Chelating agent. Succimer chelates lead and other heavy metals such as mercury and arsenic and increases their elimination from the body. Succimer is an analogue to British anti-Lewisite (BAL).

## Indications and Clinical Uses

Succimer is used for treatment of metal toxicosis, primarily toxicosis caused by lead. Other chelators that have been used for lead toxicity include calcium-EDTA, BAL, and penicillamine. Calcium-EDTA is often the preferred drug for initial treatment. The advantages of succimer over other chelators are that it is better tolerated with fewer GI adverse effects and it is not associated with nephrotoxicosis. It also does not bind other minerals such as copper, zinc, calcium, and iron.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse effects have been reported in dogs. However, kidney injury has been associated with succimer treatment in cats.

#### Contraindications and Precautions

No contraindications have been reported for animals.

#### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

Doses cited are based on studies in dogs. In cats, succimer has been used at 10 mg/kg q8h PO for 2 weeks.

## Patient Monitoring and Laboratory Tests

Monitor patient's blood lead levels during treatment. Monitor renal function during treatment because renal failure has been associated with succimer administration in cats.

## Formulations

- Succimer is available in 100-mg capsules.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 10 mg/kg q8h PO for 5 days, then 10 mg/kg q12h PO for 2 more weeks. It has also been administered rectally in vomiting dogs.

### Cats

- 10 mg/kg q8h PO for 2 weeks.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Sucralfate

soo-krahl'fate

**Trade and other names:** Carafate and Sulcrate (in Canada)

**Functional classification:** Antiulcer agent

### Pharmacology and Mechanism of Action

Gastric mucosa protectant. Antiulcer agent. Sucralfate dissociates in the stomach to form sucrose octasulfate and aluminum hydroxide. Sucrose octasulfate polymerizes to a viscous, sticky substance that creates a protective effect by binding to ulcerated mucosa. It has an affinity for negatively charged injured tissue. It protects the mucosa by preventing back-diffusion of hydrogen ions and inactivates pepsin and adsorbs bile acid. There is some evidence that sucralfate may act as a cytoprotectant (via increasing prostaglandin synthesis), but it is not certain that this is relevant to the clinical effects in dogs and cats.

### Indications and Clinical Uses

Sucralfate is used to prevent and treat gastric ulcers. However, in clinical use, there is little evidence that it will prevent ulcers from NSAIDs, although experimental evidence is available for horses. Sucralfate is administered orally and may protect ulcerated tissue and promote healing. Dosage regimens for sucralfate have been extrapolated from human dosages.

### Precautionary Information

#### Adverse Reactions and Side Effects

Because sucralfate is not absorbed, it is virtually free of adverse effects. The most common side effect associated with its use in people has been constipation.

#### Contraindications and Precautions

No contraindications have been listed for animals. Administration of intact tablets may not be effective (see [Instructions for Use](#)).

#### Drug Interactions

Sucralfate may decrease absorption of other drugs administered orally via chelation with aluminum (such as fluoroquinolones and tetracyclines). Administer these other drugs at least 30 minutes to 2 hours before sucralfate. If mixed with other drugs (antimicrobials), inactivation may occur.

### Instructions for Use

Dosing recommendations are based largely on empiricism. There are no clinical studies to demonstrate efficacy in animals with sucralfate. Sucralfate may be administered concurrently with histamine type 2 inhibitors ( $H_2$  blockers) (e.g., cimetidine) without causing an interaction. There is evidence that when intact sucralfate tablets are administered to animals, they may not undergo dissolution in the stomach and pass through the intestine intact. Therefore, it is recommended to crush up tablets and mix with a suspension prior to administration.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Sucralfate is available in 1-g tablets and a 200-mg/mL oral suspension.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Sucralfate is insoluble in water, unless exposed to strong acid or alkaline conditions. The tablets may be crushed and suspended in water to a concentration of 200 mg/mL and stored in the refrigerator for 14 days. Shake this suspension before using.

**Small Animal Dosage****Dogs**

- 0.5-1 g q8-12h PO.

**Cats**

- 0.25 g (one-fourth tablet) q8-12h PO.

**Large Animal Dosage****Foals**

- 1 g q8h PO.

**Regulatory Information**

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

**Sufentanil Citrate**

soo-fen'tah-nil sih'trate

**Trade and other names:** Sufenta

**Functional classification:** Analgesic, opioid

**Pharmacology and Mechanism of Action**

Opioid agonist. Action of fentanyl derivatives is via mu-opiate receptor. Sufentanil is 5 to 7 times more potent than fentanyl, and in some studies it is as much as 10 times more potent than fentanyl. Doses of 13-20 mcg of sufentanil produce analgesia equal to 10 mg of morphine.

**Indications and Clinical Uses**

Sufentanil, like other opiate derivatives, is used for sedation, general anesthesia, and analgesia. It can be used as part of a regimen for balanced general anesthesia. It can be used with other agents or as a primary agent in patients intubated and delivered oxygen. Sufentanil has a rapid onset of effect and rapid recovery. It does not accumulate in tissues; therefore recovery is rapid following an anesthetic procedure. It can also be administered by the epidural route. Compared to other opioids, the use of sufentanil has been limited in animals.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are similar to morphine. Like all opiates, side effects are predictable and unavoidable. Side effects include sedation, constipation, and bradycardia. Respiratory depression occurs with high doses.

**Contraindications and Precautions**

Use cautiously in animals with respiratory disease. Because of its high potency compared with morphine and other opiates, calculate dose carefully.

**Drug Interactions**

Like other opiates, sufentanil may potentiate other sedatives and anesthetics.

## Instructions for Use

When used for anesthesia, animals are often premedicated with acepromazine or a benzodiazepine.

## Patient Monitoring and Laboratory Tests

Monitor patient's heart rate and respiration. Although bradycardia rarely needs to be treated when it is caused by an opioid, atropine can be administered if necessary. If serious respiratory depression occurs, the opioid can be reversed with naloxone.

## Formulations

- Sufentanil is available in a 50-mcg/mL injection in ampules of 1, 2, and 5 mL.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated. Sufentanil is a Schedule II drug and should be stored in a locked compartment.

## Small Animal Dosage

### Dogs and Cats

- 2 mcg/kg IV (0.002 mg/kg) up to a maximum dose of 5 mcg/kg (0.005 mg/kg).

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Schedule II controlled drug.

Avoid use in animals intended for food. Withdrawal times are not established. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 1

## Sulfachlorpyridazine

sul-fah-klor-peer-id'ah-zeen

**Trade and other names:** Vetsulid

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Sulfonamide antibacterial. Sulfonamides compete with paraaminobenzoic acid (PABA) for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

## Indications and Clinical Uses

Sulfachlorpyridazine is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms. Infections treated may include pneumonia, intestinal infections (especially coccidia), soft tissue infections, and urinary tract infections (UTIs). However, resistance is common. The use of sulfachlorpyridazine has not been reported for small animals. It is used primarily for pigs and cattle. However, other drugs may be equally effective.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects associated with sulfonamides (primarily in dogs) include allergic reactions, Type II and Type III hypersensitivity, hepatotoxicity, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions.

**Contraindications and Precautions**

Do not administer in animals with sensitivity to sulfonamides.

**Drug Interactions**

Several interactions have been reported for sulfonamide administration in small animals. (See [sulfonamide](#) monographs.) However, these interactions have not been relevant for its use in cattle and pigs.

**Instructions for Use**

The most common use of sulfachlorpyridazine is for treatment of enteritis in pigs and calves.

**Patient Monitoring and Laboratory Tests**

Sulfonamides are known to decrease thyroxine ( $T_4$ ) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) break point for sensitive organisms is  $\leq 256$  mcg/mL. One sulfonamide can be used as a marker for susceptibility to other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

**Formulations**

- Sulfachlorpyridazine is available in a 2-g bolus and a 200-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage**

- No doses reported for dogs and cats.

**Large Animal Dosage****Cattle**

- 33-50 mg/kg q12h PO or IV.

**Pigs**

- 22-39 mg/kg q12h PO or 44-77 mg/kg/day PO in the drinking water.

**Regulatory Information**

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age.

Cattle withdrawal time for meat: 7 days.

Pig withdrawal time for meat: 4 days.

## Sulfadiazine

sul-fa-dye'a-zeen

**Trade and other names:** Generic brands and combined with trimethoprim as Tribissen and Equisul-SDT

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Sulfonamide antibacterial. Sulfonamides compete with PABA for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

### Indications and Clinical Uses

Sulfadiazine is used alone occasionally; however, efficacy is not established for many infections. Most often, it is used with trimethoprim to treat a variety of infections, including UTIs and skin infections. (See monograph on trimethoprim-sulfonamides in this book for a more complete description.)

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other more toxic metabolites may persist.

#### Contraindications and Precautions

Do not administer to animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed.

#### Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde that may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for IV forms of trimethoprim-sulfonamides.

### Instructions for Use

Usually, sulfonamides are combined with trimethoprim or ormetoprim in a 5:1 ratio, and sulfonamides are rarely used alone in small animals and horses. There is no clinical evidence that one sulfonamide is more or less toxic or efficacious than another sulfonamide.



### Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease thyroxine ( $T_4$ ) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 256$  mcg/mL. One sulfonamide can be used as a marker for susceptibility to other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

### Formulations

- Sulfadiazine is available in 500-mg tablets. See monograph on trimethoprim-sulfadiazine for information on those formulations.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 100 mg/kg IV PO (loading dose), followed by 50 mg/kg q12h IV or PO (see also trimethoprim).

### Large Animal Dosage

- For horses, see dosing for trimethoprim combinations.

### Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age. No withdrawal times are established. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Sulfadimethoxine

sul-fah-dye-meth-oks'een

**Trade and other names:** Albon, Bactrovet, and generic brands

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Sulfonamide antibacterial. Sulfonamides compete with PABA for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

### Indications and Clinical Uses

Sulfadimethoxine is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms. Infections treated may include pneumonia, intestinal infections (especially coccidia), soft tissue infections, and UTIs. However resistance is common, unless combined with ormetoprim (see Primor).

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other more toxic metabolites may persist.

### Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed.

### Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde that may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for IV forms of trimethoprim-sulfonamides.

## Instructions for Use

Usually, sulfonamides are combined with trimethoprim or ormetoprim in a 5:1 ratio, and sulfonamides are rarely used alone in small animals and horses. There is no clinical evidence that one sulfonamide is more or less toxic or efficacious than another sulfonamide. Sulfadimethoxine has been combined with ormetoprim in Primor.

## Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease thyroxine ( $T_4$ ) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 256$  mcg/mL. One sulfonamide can be used as a marker for susceptibility to other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

## Formulations

- Sulfadimethoxine is available in 125-, 250-, and 500-mg tablets; 400-mg/mL injection; and 50-mg/mL suspension.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 55 mg/kg PO (loading dose), followed by 27.5 mg/kg q12h PO. (For doses of combination with ormetoprim, see Primor.)

## Large Animal Dosage

### Cattle

- Treatment of pneumonia and other infections: 55 mg/kg as initial dose, followed by 27 mg/kg q24h PO for 5 days.
- Sustained-release bolus (Albon-SR): 137.5 mg/kg PO as a single dose.

## Regulatory Information

Cattle withdrawal time for meat: 7 days.

Cattle withdrawal time for milk: 60 hours.

Withdrawal time for sustained-released bolus: 21 days.

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age. Currently sulfadimethoxine is the only sulfonamide with approved indications in dairy cattle.

## Sulfamethazine

sul-fah-meth'ah-zeen

**Trade and other names:** Sulmet and generic brands

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Sulfonamide antibacterial. Sulfonamides compete with PABA for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

## Indications and Clinical Uses

Sulfamethazine is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms. Infections treated may include pneumonia, intestinal infections (especially coccidia), soft tissue infections, and UTIs. However, resistance is common.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects associated with sulfonamides include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other more toxic metabolites may persist.

### Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed.

### Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapson, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for IV forms of trimethoprim-sulfonamides.

### Instructions for Use

Usually sulfonamides are combined with trimethoprim or ormetoprim in a 5:1 ratio, and sulfonamides are rarely used alone in small animals and horses that have other preexisting disease such as liver failure. There is no clinical evidence that one sulfonamide is more or less toxic or efficacious than another sulfonamide.

### Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease thyroxine ( $T_4$ ) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 256$  mcg/mL. One sulfonamide can be used as a marker for susceptibility to other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

### Formulations

- Sulfamethazine is available in a 30-g bolus.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 100 mg/kg PO (loading dose), followed by 50 mg/kg q12h PO.

### Large Animal Dosage

#### Cattle

- Treatment of pneumonia and other infections: 220 mg/kg as initial dose, followed by 110 mg/kg q24h PO.
- Use of soluble powder as a drench or in drinking water: 237 mg/kg as initial dose, followed by 119 mg/kg q24h PO.
- Sustained-release bolus: 350-400 mg/kg PO as a single dose.

#### Pigs

- Use of soluble powder as a drench or in drinking water: 237 mg/kg as initial dose, followed by 119 mg/kg q24h PO.

### Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle greater than 20 months of age.

Cattle withdrawal time for meat: 10 or 11 days.

Cattle withdrawal time for meat (soluble powder): 10 days.

Pig withdrawal time for meat (soluble powder): 15 days.

Cattle withdrawal time for meat (sustained-release bolus): 8-18 days, depending on the product.

## Sulfamethoxazole

sul-fah-meth-oks'ah-zole

**Trade and other names:** Gantanol

**Functional classification:** Antibacterial

**Note:**

This drug has been discontinued and is no longer available. Consult earlier editions of this book for information on the pharmacology, mechanism of action, and clinical use.

**Sulfaquinoxaline**

sul-fah-kwin-oks'ah-leen

**Trade and other names:** Sulfa-Nox

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Sulfonamide antibacterial. Sulfonamides compete with PABA for an enzyme that synthesizes dihydrofolic acid in bacteria. It is synergistic with trimethoprim. Bacteriostatic. Like other sulfonamides, it has a broad spectrum of activity, including gram-positive bacteria, gram-negative bacteria, and some protozoa. However, when used alone, resistance is common.

**Indications and Clinical Uses**

Sulfaquinoxaline is used as a broad-spectrum antimicrobial to treat or prevent infections caused by susceptible organisms. Infections treated may include pneumonia, intestinal infections (especially coccidia), soft tissue infections, and UTIs. However, resistance is common.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects associated with sulfonamides include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites. Other more toxic metabolites may persist.

**Contraindications and Precautions**

Do not administer in animals with sensitivity to sulfonamides. Avoid contact with skin or mucous membranes when mixing in water.

**Drug Interactions**

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde that may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for IV forms of trimethoprim-sulfonamides.

**Instructions for Use**

Mix in the drinking water. Make fresh solutions daily. The most common use of sulfaquinoxaline is for treatment of enteritis caused by coccidia in calves, sheep, and poultry.

## Patient Monitoring and Laboratory Tests

Sulfonamides are known to decrease thyroxine ( $T_4$ ) concentrations in dogs after 6 weeks of treatment. Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 256$  mcg/mL. One sulfonamide can be used as a marker for susceptibility to other sulfonamides. According to CLSI, susceptibility tests for sulfonamides can be used to interpret urinary bacteria isolates only.

## Formulations

- Sulfaquinoxaline is available in 34.4-, 128.5-, 192-, 200-, 286.2-, and 340-mg/mL solution.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

- No doses reported for dogs and cats.

## Large Animal Dosage

### Calves

- 13.2 mg/kg/day PO (usually administered in the drinking water as a 0.015% solution for 5 days).

## Regulatory Information

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle greater than 20 months of age.

Cattle withdrawal time: 10 days.

Sheep withdrawal time: 10 days.

Poultry withdrawal time: 10 days.

Rabbit withdrawal time: 10 days.

## Sulfasalazine

sul-fah-sal'ah-zeen

**Trade and other names:** Azulfidine and Salazopyrin (in Canada)

**Functional classification:** Antibacterial

## Pharmacology and Mechanism of Action

Sulfonamide combined with an anti-inflammatory drug. Sulfasalazine has little effect, and salicylic acid (mesalamine) has anti-inflammatory effects. (See monograph for mesalamine in this book for more details on its use.) When administered as the combination of salicylic acid and the sulfonamide sulfapyridine, the salicylic acid is released by colonic bacteria to produce an anti-inflammatory effect. The anti-inflammatory effect is believed to be through antiprostaglandin action, antileukotriene activity, or both.

## Indications and Clinical Uses

Sulfasalazine is used in small animals for the treatment of idiopathic colitis and other inflammatory intestinal diseases. It is often the first drug of choice for treatment when dietary therapy has been unsuccessful. Although sulfasalazine has been commonly used in small animals, use in animals has been primarily derived from empirical use. There are no well-controlled clinical studies or efficacy trials to document

clinical effectiveness. The monograph on mesalamine in this book has additional information on clinical use.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects are all attributed to the sulfonamide component. Adverse effects are associated with sulfonamides and include allergic reactions, Type II and Type III hypersensitivity, hypothyroidism (with prolonged therapy), keratoconjunctivitis sicca, and skin reactions. Keratoconjunctivitis sicca has been reported in dogs that received sulfasalazine for chronic treatment. The amount of salicylate absorbed appears to be small in cats; therefore adverse effects from salicylate in cats are unlikely.

#### **Contraindications and Precautions**

Do not administer to animals that are sensitive to sulfonamides. Drug interactions are possible but have not been reported in animals, probably because low systemic drug concentrations are achieved. Mesalamine can potentially interfere with thiopurine methyltransferase and therefore increase the risk of toxicity from azathioprine.

#### **Drug Interactions**

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides.

### **Instructions for Use**

Usually used for treatment of idiopathic colitis, often in combination with dietary therapy. For animals sensitive to sulfonamides, consider other forms of mesalamine (see mesalamine monograph for more details).

### **Patient Monitoring and Laboratory Tests**

Monitor tear production in dogs that receive chronic therapy.

### **Formulations**

- Sulfasalazine is available in 500-mg tablets and has been compounded as an oral suspension for smaller animals.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### **Small Animal Dosage**

#### **Dogs**

- 10-30 mg/kg q8-12h PO.

#### **Cats**

- 20 mg/kg q12h PO.

### **Large Animal Dosage**

- No doses have been reported for large animals.

### **Regulatory Information**

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle older than 20 months of age.

RCI Classification: 4

## Tacrolimus

tak-roe-lih'mus

**Trade and other names:** Protopic, FK506

**Functional classification:** Immunosuppressant

### Pharmacology and Mechanism of Action

Tacrolimus is a microbial product isolated from the organism *Streptomyces tsukubaensis*. It binds to an intracellular receptor and subsequently binds to calcineurin and inhibits the calcineurin pathway that stimulates the nuclear factor, NFAT. The action resembles that of cyclosporine (both drugs are calcineurin inhibitors), although the cellular receptors differ. By inhibiting the action of NFAT, tacrolimus decreases synthesis of inflammatory cytokines. In particular, synthesis of interleukin-2 (IL-2) is inhibited, which results in decreased activation of T-lymphocytes. It is 10-100 times more potent than cyclosporine. Tacrolimus inhibits release of mast cell and basophil mediators and decreases inflammatory mediator expression.

### Indications and Clinical Uses

Tacrolimus is used as an immunosuppressive drug to treat autoimmune disease, prevent organ transplant rejection, and treat atopic dermatitis. Most use in animals is with a topical formulation. It has been applied topically (ointment) for localized areas of atopic dermatitis or on skin areas of dogs where local immunosuppressive treatment is needed (e.g., on the bridge of the nose). In some cases after resolution of lesions with systemic treatment with cyclosporine, isolated skin lesions are managed topically with tacrolimus ointment. There has been limited use for preventing renal transplant rejection in cats because the pharmacokinetics have been highly variable. A related drug, pimecrolimus, also has been used topically.

### Precautionary Information

#### Adverse Reactions and Side Effects

There may be a slight burning or pruritic sensation with initial topical application. These reactions are mild and decrease as the skin heals. With systemic administration, dogs may show gastrointestinal (GI) signs, which include diarrhea, intestinal discomfort, vomiting, intestinal intussusception, and intestinal injury. Tacrolimus is minimally absorbed systemically from topical application.

#### Contraindications and Precautions

Tacrolimus is a potent immunosuppressant. Use cautiously in animals prone to infection. Pet owners should be cautioned about skin contact when handling the medication for their pets.

#### Drug Interactions

No drug interactions have been identified from topical administration.

### Instructions for Use

There are no reports of safe systemic doses used in dogs. Most use is topical. It can be used topically for immune-mediated skin lesions where local treatment can be used (e.g., on the bridge of the nose). It has also been applied topically for perianal fistula in addition to systemic prednisolone.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary with topical use.



**Formulations Available**

- Tacrolimus is available in 0.1% and 0.03% topical ointment in 30-, 60-, and 100-g tubes.

**Stability and Storage**

Ointment is stable if stored in manufacturer's original formulation. Compounded formulations of tacrolimus have been available from pharmacists, but the stability and potency of these formulations have not been evaluated. It is practically insoluble in water. When prepared in a suspension, it was stable for several weeks.

**Small Animal Dosage****Dogs and Cats**

- Apply topical ointment (0.1%) to localized lesions on affected areas of skin. It has been used in dogs twice daily. For perianal fistula, it has been applied twice daily.

**Large Animal Dosage**

- No doses have been reported for large animals.

**Regulatory Information**

Do not administer to animals intended for food.

**Tegaserod Maleate**

teg-ah-ser'-odd mal'-ee-ate

**Trade and other names:** Zelnorm

**Functional classification:** Gastrointestinal stimulant

**Notice:**

In 2007, tegaserod was removed from the US market and was made available to physicians only through a restricted distribution program from the manufacturer. Beginning in April 2008, tegaserod was no longer available through the restricted distribution program; therefore the US Food and Drug Administration (FDA) has decided to make tegaserod available to physicians for patients in emergency situations that are life threatening or require hospitalization.

Thus this drug is no longer available to veterinarians. For information on the pharmacology, use, and dosing for tegaserod, please consult previous editions of this book.

**Tamoxifen Citrate**

tah-moks'ih-fen sih'trate

**Trade and other names:** Nolvadex

**Functional classification:** Antiestrogen

**Pharmacology and Mechanism of Action**

Nonsteroidal estrogen receptor blocker. Tamoxifen also has weak estrogenic effects. It also increases release of gonadotropin-releasing hormone (GnRH).

## Indications and Clinical Uses

Tamoxifen is used as adjunctive treatment for certain tumors, especially estrogen-responsive tumors. The most common use in animals is adjunctive treatment for mammary neoplasia. In women, it has been used to induce ovulation by stimulating release of GnRH from the hypothalamus.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been thoroughly documented in animals. However, in people, tamoxifen has been reported to cause increased tumor pain.

#### Contraindications and Precautions

Do not use in pregnant animals.

#### Drug Interactions

Tamoxifen is a potent cytochrome P450 enzyme inhibitor. It may interact with other drugs that are Cytochrome P450 substrates.

## Instructions for Use

Tamoxifen is often used with other anticancer drug protocols.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations Available

- Tamoxifen is available in 10- and 20-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

- Veterinary dose not established but has been extrapolated from the human dose. Human dose is 10 mg q12h PO (approximately 0.14 mg/kg q12h).

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

## Taurine

tore'een

**Trade and other names:** Generic brands

**Functional classification:** Nutritional supplement

## Pharmacology and Mechanism of Action

Nutritional supplement. Taurine is a naturally occurring amino acid considered essential for cats. Deficiencies in animals may lead to blindness and heart disease. Taurine may have some cardiac inotropic effects.

## Indications and Clinical Uses

Taurine is used in the prevention and treatment of ocular and cardiac disease (dilated cardiomyopathy) caused by taurine deficiency. Although current commercial diets

have adequate amounts of taurine, it has been supplemented in dogs and cats with heart disease.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects have not been reported.

#### **Contraindications and Precautions**

No contraindications are reported for animals.

#### **Drug Interactions**

No drug interactions have been reported in animals.

### **Instructions for Use**

Routine supplementation with taurine may not be necessary in animals that are receiving a balanced diet. However, supplementation may be necessary in animals with diseases associated with taurine deficiency.

### **Patient Monitoring and Laboratory Tests**

Taurine concentrations can be measured in some laboratories to detect deficiencies. Normal levels in plasma are 60-120 nmol/mL in dogs and cats or 200-350 nmol/mL in whole blood. Levels below 40 nmol/mL in plasma and 150 nmol/mL in whole blood are considered deficient.

### **Formulations Available**

- Taurine is available in powder or supplemented in some diets. Consult a compounding pharmacy for availability.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

### **Small Animal Dosage**

#### **Dogs**

- 500 mg/dog q12h PO.

#### **Cats**

- 250 mg/cat q12h PO.

### **Large Animal Dosage**

No doses have been reported for large animals.

### **Regulatory Information**

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## **Telmisartan**

Tel'-mi-Sar'-tan

**Trade and other names:** Micardis

**Functional classification:** Vasodilator

### **Pharmacology and Mechanism of Action**

Vasodilator, angiotensin II receptor blocker (ARB). It has high affinity and selectivity for the AT1 receptor. The action is similar to that of angiotensin-converting enzyme

(ACE) inhibitors, except that it directly blocks the receptor, rather than inhibits synthesis of angiotensin II. Angiotensin II receptor blockers have the advantage of being less likely to induce hyperkalemia and are more easily tolerated in people. Telmisartan and other ARBs have been used in people who cannot tolerate ACE inhibitors.

In dogs, telmisartan has a longer half-life and is more lipophilic than other ARBs (half-life up to 15 hours) and may be administered in dogs once daily.

### Indications and Clinical Uses

In dogs, clinical experience with telmisartan and other ARB drugs is limited. Ordinarily ACE inhibitors are used first (e.g., enalapril, benazepril). However, in experimental dogs, telmisartan (1 mg/kg) was more effective than enalapril. If it is necessary to directly block the angiotensin receptor, telmisartan and other drugs in this class may be indicated. A related drug, irbesartan (30 mg/kg q12h), has also been shown to block angiotensin II receptors in dogs. Another ARB, losartan, has been used in dogs, but it is less potent because it relies mostly on an active metabolite that dogs do not produce (see section on Losartan in this book for more details). There are no well-controlled clinical trials testing the effectiveness of telmisartan or other ARB drugs in dogs. The use is based on studies in experimental animals and anecdotal experience.

### Precautionary Information

#### Adverse Reactions and Side Effects

No adverse reactions have been reported in animals. In people, hypotension may occur.

#### Contraindications and Precautions

No specific contraindications have been reported for animals. Do not use in pregnant animals.

#### Drug Interactions

Combined use of an ARB and an ACE inhibitor may increase risk of kidney injury because of dual blockade. This may be associated with increased risks of hypotension, hyperkalemia, and changes in kidney function.

### Instructions for Use

In dogs, telmisartan is more active than losartan, which must be converted to an active metabolite. Telmisartan has a longer half-life than other drugs in this class.

### Patient Monitoring and Laboratory Tests

Monitor blood pressure in treated animals.

### Formulations

- Losartan is available in 20-, 40-, and 80-mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 1 mg/kg once per day PO as a starting dose. Increase to 3 mg/kg once per day and then to twice daily, if needed.

#### Cats

- No dose established.

### Large Animal Dosage

- No large animal doses have been reported.

**Regulatory Information**

Do not administer to animals intended for food.

Racing Commissioners International (RCI) Classification: 3

**Tepoxalin**

tep-oks'ah-lin

**Trade and other names:** Zubrin

**Functional classification:** Anti-inflammatory

**Note:** Although this is still an FDA-approved drug, the manufacturer has voluntarily withdrawn tepoxalin from the veterinary market in the US. Information is included regarding pharmacology, indications, and dosing in the event that it may return to the market in the future.

**Pharmacology and Mechanism of Action**

Tepoxalin is a nonsteroidal anti-inflammatory drug (NSAID). Like other drugs in this class, it produces analgesic and anti-inflammatory effects by inhibiting the synthesis of prostaglandins. However, tepoxalin also inhibits the action of lipoxygenase (LOX) to decrease synthesis of inflammatory leukotrienes in dogs. This produces a “dual action” in dogs by inhibiting both prostaglandins and leukotrienes. Tepoxalin, using in vitro assays, is more cyclooxygenase-1 (COX-1) selective than COX-2 selective. It has not been established if the specificity for COX-1 or COX-2 is related to efficacy or safety. Tepoxalin forms an active metabolite after administration to dogs, cats, and horses. In dogs, tepoxalin has a half-life of 2 hours and the acid metabolite has a half-life of 13 hours. It is highly protein bound. Feeding increases oral absorption in dogs.

**Indications and Clinical Uses**

Tepoxalin has been used for the acute and chronic treatment of pain and inflammation in dogs. One of the most common uses is osteoarthritis, but it also has been used for pain associated with surgery. There is evidence that it was more effective than carprofen or meloxicam for reducing intraarticular inflammation in dogs and controlling synthesis of intraarticular PGE<sub>2</sub>. Because of the dual action of tepoxalin, it has been investigated for treating other inflammatory conditions in dogs and cats. Studies available thus far to investigate the beneficial effect of dual inhibition by tepoxalin for other inflammatory diseases (for example, ocular inflammation, respiratory disease, or dermatitis) have had mixed results. Tepoxalin has been more effective than other drugs for ocular inflammation, but only partially effective for dermatitis, and is not effective for respiratory disease. Use in large animals has not been reported.

**Precautionary Information****Adverse Reactions and Side Effects**

Gastrointestinal problems are the most common adverse effects associated with tepoxalin and can include vomiting, diarrhea, nausea, ulcers, and erosions of the GI tract. Both acute and long-term safety and efficacy have been established for dogs. In field trials, vomiting was the most often reported adverse effect. In studies performed in dogs, they have tolerated 10 times and 30 times the labeled

dose. Renal effects and bleeding studies have been performed on healthy dogs. In these studies tepoxalin was not shown to adversely affect bleeding times or renal function. Nevertheless, renal toxicity, especially in dehydrated animals or animals with preexisting renal disease, has been shown for some NSAIDs. Toxicity studies have not been performed in cats, but single doses of 10 mg/kg to a small group of cats did not produce adverse effects.

### **Contraindications and Precautions**

Dogs and cats with preexisting GI problems or kidney disease may be at a greater risk of adverse effects from NSAIDs. Safety in pregnancy is not known, but adverse effects have not been reported.

### **Drug Interactions**

Do not administer with other NSAIDs or with corticosteroids. Corticosteroids have been shown to exacerbate the GI adverse effects. Some NSAIDs may interfere with the action of diuretic drugs ACE inhibitors. However, in experimental studies in dogs, tepoxalin combined with an ACE inhibitor did not produce adverse renal effects.

## **Instructions for Use**

Rapidly dissolving tablets can be administered with or without food. In some animals, it is helpful to wet the tablet before placing on the animal's tongue. Long-term studies have not been completed in cats; only single-dose studies have been reported in which a dose of 10 mg/kg did not produce adverse effects.

## **Patient Monitoring and Laboratory Tests**

Monitor GI signs for evidence of diarrhea, GI bleeding, or ulcers. Because of risk of kidney injury, monitor renal parameters (water consumption, blood urea nitrogen [BUN], creatinine, and urine-specific gravity) periodically during treatment.

## **Formulations**

- Tepoxalin was previously available in 30-, 50-, 100-, and 200-mg tablets (rapidly dissolving).

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Shelf life is 2 years if maintained in manufacturer's original packaging.

## **Small Animal Dosage**

### **Dogs**

- 10 mg/kg q24h PO. It is safe to start with 20 mg/kg initially and use a dose of 10-20 mg/kg because of its wide safety margin.

### **Cats**

- Cats have tolerated 10 mg/kg as a single dose, but long-term safety has not been evaluated.

## **Large Animal Dosage**

- No doses have been reported for large animals.

## **Regulatory Information**

Do not administer to animals that produce food.

## Terbinafine Hydrochloride

ter-bin'ah-feen hye-droe-klor'ide

**Trade and other names:** Lamisil

**Functional classification:** Antifungal

### Pharmacology and Mechanism of Action

Antifungal drug. Terbinafine belongs to the allylamine group of antifungal drugs. It acts on ergosterol biosynthesis by targeting fungal squalene epoxidase (SE). Squalene epoxidase is a membrane-bound enzyme and is involved in the conversion of squalene into squalene 2,3-epoxide, which is subsequently converted into lanosterol and ergosterol. Terbinafine is selective for fungal SE.

Terbinafine is active against yeasts and a wide range of dermatophytes with a low minimum inhibitory concentration (MIC) of 0.01 mcg/mL or less. It is fungicidal against *Trichophyton* spp., *Microsporum* spp., and *Aspergillus* spp. It is also active against *Blastomyces dermatitidis*, *Cryptococcus neoformans*, *Sporothrix schenckii*, *Histoplasma capsulatum*, *Candida*, and *Malassezia pachydermatis* yeast. There may be some activity against protozoa (e.g., *Toxoplasma*). Despite the in vitro activity listed here, there are not enough data on clinical response from these infections to recommend terbinafine over other more traditional treatments in animals.

Terbinafine is active based on in vitro tests against dermatophytes.

Oral bioavailability in most animals is high, ranging from 31% in cats to >46% in dogs. The half-life in dogs and cats is 8.6 and 8.1 hours, respectively. Oral absorption in horses is low compared with dogs and it is not recommended for oral treatment in horses. Because of its lipophilicity, high concentrations are attained in tissues such as stratum corneum, hair follicles, sebum-rich skin, and nails. In people, after 12 days of therapy, the concentrations in stratum corneum exceed those in plasma by a factor of 75. In cats after a daily dose of 30-40 mg/kg, the concentrations in hair persist for 5 weeks after discontinuation of treatment at 14 days.

### Indications and Clinical Uses

Terbinafine is indicated for treatment of dermatophyte infections in dogs, cats, birds, and some exotic animals. For dermatophytes in animals, the doses necessary for efficacy are much higher than those used in people. Although there has been experience with using terbinafine in animals—primarily for dermatophytes—there is no evidence that terbinafine is more effective than other oral antifungal agents. In dogs it is effective for the treatment of *Malassezia* dermatitis when given at 30 mg/kg PO once a day or twice a week for at least 3 weeks. However, this treatment produced insufficient resolution and only partial remission even though there was clinical improvement. In cats after 14 days of treatment, it persists in the hair for as long as 5 weeks, but in some populations of cats (e.g., shelter cats), it has not been consistently effective for dermatophyte infections. Treatment of infections in horses with terbinafine has not been successful, probably because of poor absorption.

### Precautionary Information

#### Adverse Reactions and Side Effects

Vomiting has been the most common adverse effect. Adverse effects, including nausea and anorexia, have been observed in dogs. Liver enzymes may be elevated in some animals. Hepatotoxicity is possible, but it has not been reported from use

in animals. Facial pruritus has been observed in some treated cats. In people, a persistent taste disturbance, GI problems, and headache have been reported.

### **Contraindications and Precautions**

No contraindications have been reported for animals.

### **Drug Interactions**

No drug interactions have been reported in animals.

## **Instructions for Use**

Treatment of dogs and cats requires much higher doses compared with doses used in people. Despite the in vitro activity of terbinafine against many fungi and the favorable pharmacokinetics in dogs and cats, the clinical results have not consistently produced clinical resolution in some patients.

## **Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

## **Formulations**

- Terbinafine is available in 250-mg tablets, 1% topical solution, and 1% topical cream.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Terbinafine is slightly soluble in water and alcohol. When suspensions have been prepared from crushed tablets in a vehicle (Ora-Sweet), it was stable for 42 days.

## **Small Animal Dosage**

### **Dogs**

- 30-40 mg/kg q24h PO (with food) for 2-3 weeks.

### **Cats**

- 30-40 mg/kg/day PO for at least 2 weeks. Or, administer one-quarter tablet for small cats (62.5 mg), one-half tablet for medium-size cats (125 mg), and one tablet for large cats (250 mg), all administered once daily.

## **Large Animal Dosage**

There are no effective doses reported for large animals. It is not effective for horses.

## **Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

## **Terbutaline Sulfate**

ter-byoo'tah-leen sul'fate

**Trade and other names:** Brethine and Bricanyl

**Functional classification:** Bronchodilator, beta agonist



## Pharmacology and Mechanism of Action

Beta<sub>2</sub>-adrenergic agonist. Bronchodilator. Stimulates beta<sub>2</sub>-receptors to relax bronchial smooth muscle. Terbutaline is more beta<sub>2</sub> specific than drugs such as isoproterenol. Other beta<sub>2</sub>-specific drugs include albuterol and metaproterenol. In addition to the beta<sub>2</sub> effects to relax bronchial smooth muscle and relieve bronchospasm, the beta<sub>2</sub>-agonists may inhibit release of inflammatory mediators, especially from mast cells.

## Indications and Clinical Uses

Terbutaline, like other beta<sub>2</sub>-agonists, is indicated in animals with reversible bronchoconstriction, such as cats with bronchial asthma. It also has been used in dogs to relieve bronchoconstriction and in animals with bronchitis and other airway diseases. It has been used in horses for short-term administration, by injection, to relieve bronchoconstriction associated with recurrent airway obstruction (RAO). Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Albuterol injection may be used as an alternative for terbutaline injection (4 mcg/kg bolus up to 8 mcg/kg as needed). Terbutaline is not absorbed by the oral route in horses; therefore it is not effective in horses for oral administration. Clenbuterol usually is the drug of choice for horses.

## Precautionary Information

### Adverse Reactions and Side Effects

Excessive beta-adrenergic stimulation from terbutaline at high doses results in tachycardia and muscle tremors. Arrhythmias are possible with high doses. All beta<sub>2</sub>-agonists will inhibit uterine contractions at the end of gestation in pregnant animals. High doses of beta<sub>2</sub>-agonists can lead to hypokalemia because they stimulate Na<sup>+</sup>-K<sup>+</sup>-ATPase and increase intracellular K<sup>+</sup> while decreasing serum K<sup>+</sup> and producing hyperglycemia. Treatment consists of KCl supplement at a rate of 0.5 mEq/kg/hr.

### Contraindications and Precautions

Administer cautiously to animals with cardiac disease, particularly animals that may be susceptible to tachyarrhythmias. Do not use late in gestation unless the intended effect is to delay uterine contractions.

### Drug Interactions

Use cautiously with other drugs that may stimulate the heart and cause tachycardia.

## Instructions for Use

May be administered PO, IM, or SQ. Terbutaline (and other beta<sub>2</sub>-agonists) have also been used in people to delay labor (dose in people is 2.5 mg q6h PO). Other beta<sub>2</sub>-agonists used in animals for relief of bronchoconstriction include albuterol and salmeterol. Animals with acute bronchoconstriction also may benefit from corticosteroid treatment and oxygen therapy. Caution should be used when administering repeated SQ doses. The maximum SQ dose in people is 500 mcg/person (0.5 mg) within a 4-hour period.

## Patient Monitoring and Laboratory Tests

Monitor heart rate in animals during treatment. Monitor potassium concentration if high doses are administered.

## Formulations

- Terbutaline is available in 2.5- and 5-mg tablets and 1 mg vials with a concentration of 1-mg/mL, 1-mL for injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Terbutaline sulfate is soluble in water. Solutions may be subject to degradation. Observe for color change, and discard if solution turns a dark color. Suspensions have been prepared from tablets in syrup and remained stable for 55 days.

## Small Animal Dosage

### Dogs

- 1.25-5 mg/dog q8h PO.
- 3-5 mcg/kg (0.003-0.005 mg/kg) SQ, usually as a single dose in an emergency. If necessary, repeat in 4-6 h.

### Cats

- 0.1 mg/kg q8h PO.
- 0.625 mg/cat (one quarter of 2.5-mg tablet) q12h PO.
- 5-10 mcg/kg (0.005-0.01 mg/kg) q4h SQ or IM. The most common dose in cats is 0.05 mg (equivalent to 0.05 mL) per cat injected SQ.

## Large Animal Dosage

### Horses

- Not absorbed orally. Use IV for treatment of chronic recurrent airway obstruction (RAO): 2-5 mcg/kg q6-8h IV or as needed.

## Regulatory Information

Terbutaline has similar properties as clenbuterol and should not be administered to animals intended for food.

RCI Classification: 3

## Testosterone

tess-toss'ter-one

**Trade and other names:** Testosterone cypionate ester: Andro-Cyp, Andronate, Depo-Testosterone, and generic brands and testosterone propionate ester: Testex and Malogen (in Canada)

**Functional classification:** Hormone

## Pharmacology and Mechanism of Action

Testosterone ester for injection is available in two forms: testosterone cypionate and testosterone propionate. It is used to supplement testosterone in deficient animals. It will also produce anabolic effects. Testosterone esters are administered intramuscularly to avoid first-pass effects that occur from oral administration. Esters in oil are absorbed more slowly from IM injections. Esters are then hydrolyzed to free testosterone. Other agents with more specific anabolic activity include boldenone, oxymetholone, nandrolone, stanozolol, and methyltestosterone.

## Indications and Clinical Uses

Anabolic agents have been used for reversing catabolic conditions, increasing weight gain, increasing muscling in animals, and stimulating erythropoiesis. Testosterone and other anabolic agents have also been abused in people to enhance athletic performance.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are caused by excessive androgenic action of testosterone. Prostatic hyperplasia is possible in male dogs. Masculinization can occur in female dogs. Hepatopathy is more common with oral methylated testosterone formulations than with injected formulations. In men who take excessive testosterone supplements, there are cardiovascular risks.

**Contraindications and Precautions**

Use cautiously in patients with hepatic disease. Do not administer to pregnant animals. This drug has potential for abuse in humans for anabolic uses.

**Drug Interactions**

No drug interactions have been reported in animals.

**Instructions for Use**

Use of testosterone androgens has not been evaluated in clinical studies in veterinary medicine. Use is based primarily on experimental evidence or experiences in people.

**Patient Monitoring and Laboratory Tests**

Monitor hepatic enzymes in treated patients periodically.

**Formulations**

- Testosterone cypionate ester is available in 100- and 200-mg/mL injections.
- Testosterone propionate ester is available in 100-mg/mL injections.

**Stability and Storage**

Testosterone is insoluble in water but soluble in oils and ethanol. Protect from light, heat, and freezing. When mixed with oil, it has been stable for 60 days.

**Small Animal Dosage****Dogs and Cats**

- Testosterone cypionate ester: 1-2 mg/kg q2-4 weeks IM.
- Testosterone propionate ester: 0.5-1 mg/kg 2-3 times/week IM.

**Large Animal Dosage**

There are no large animal formulations available, except for implants for calves. Do not administer injections to animals intended for food.

**Regulatory Information**

Testosterone is a Schedule III controlled drug.

RCI Classification: 4

**Tetracycline, Tetracycline Hydrochloride**

tet-rah-sye'kleen

**Trade and other names:** Panmycin, Duramycin powder, and Achromycin V

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Tetracycline antibiotic. Mechanism of action of tetracyclines is to bind to 30S ribosomal subunit and inhibit protein synthesis. The action is time dependent and against some

bacteria is bacteriostatic. Tetracycline, like other tetracyclines, has a broad spectrum of activity, including bacteria, some protozoa, *Rickettsiae*, and *Ehrlichiae*. Resistance is common. Of the tetracyclines used in animals (oxytetracycline, doxycycline) all have similar activity. However, minocycline may have better activity against some strains of *Staphylococcus* (see minocycline section in this book for more details). Tigecycline is a new tetracycline that has improved activity against bacteria that are resistant to other drugs. However, there are no reports of its use in animals.

## Indications and Clinical Uses

Tetracyclines are used to treat a variety of infections, including soft tissue infections, pneumonia, and urinary tract infections (UTIs). Tetracycline is not often used for treatment in animals, as there are few dosage forms (except topical) and other derivatives in this group are used more frequently in animals for treatment include oxytetracycline, minocycline, and doxycycline. Consult sections containing those drugs in this book for a more complete list of clinical use and indications.

## Precautionary Information

### Adverse Reactions and Side Effects

Tetracyclines in general may cause renal tubular necrosis at high doses. Tetracyclines can affect bone and teeth formation in young animals. They have been implicated in drug fever in cats. Hepatotoxicity may occur at high doses in susceptible individuals. Oral administration can cause diarrhea in some animals.

### Contraindications and Precautions

Do not use in young animals because it can affect bone and teeth formation.

### Drug Interactions

Tetracyclines bind to compounds that contain calcium, which decreases oral absorption. Do not mix with solutions that contain iron, calcium, aluminum, or magnesium.

## Instructions for Use

Pharmacokinetic and experimental studies have been conducted in small animals but not in clinical studies. Use of tetracyclines in small animals has primarily been replaced by doxycycline or minocycline. In cattle, pigs, and other large animals, the most commonly administered tetracycline is oxytetracycline, either in feed or water, or by injection. The most common oral tetracycline in horses is doxycycline or minocycline.

## Patient Monitoring and Laboratory Tests

Tetracycline can be tested as the class representative for susceptibility to chlortetracycline, doxycycline, minocycline, and oxytetracycline. Organisms that are susceptible to tetracycline are also considered susceptible to the other tetracyclines. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline or minocycline or both. Susceptibility testing: Clinical and Laboratory Standards Institute (CLSI) break point for sensitive organisms is  $\leq 2$  mcg/mL for streptococci and  $\leq 4$  mcg/mL for other organisms. However, on the basis of plasma concentrations achieved, 1 mcg/mL or less should be used for animals. When testing *Staphylococcus* spp. from dogs, the break point for susceptible isolates is  $\leq 0.25$  mcg/mL. When using tetracycline to test for susceptibility to oxytetracycline in pathogens from cattle, use a break point of  $\leq 2$  mcg/mL for susceptible bacteria. When using tetracycline to test for susceptibility to oxytetracycline in pathogens from swine, use a break point of  $\leq 0.5$  mcg/mL for susceptible bacteria.

## Formulations

- Tetracycline is available in 250- and 500-mg capsules, 500-mg calf bolus, 100-mg/mL oral suspension, and 25 and 324 g/lb of powder.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Tetracycline has poor aqueous solubility. However, tetracycline hydrochloride is more soluble (100 mg/mL). The pH of tetracycline hydrochloride solution is approximately 2.0. It will decompose if kept at alkaline pH. Tetracycline hydrochloride is unstable, and compounded preparations are better prepared from tetracycline base as a suspension. Tetracycline will darken with exposure to light. Protect from freezing.

## Small Animal Dosage

### Dogs and Cats

- 15-20 mg/kg q8h PO.
- 4.4-11 mg/kg q8h IV or IM.
- Rickettsial infection (dogs): 22 mg/kg q8h for 14 days PO.

## Large Animal Dosage

### Calves and Pigs

- For treatment of enteritis and pneumonia: 11 mg/kg q12h, or 22 mg/kg once daily administered in the water or as a bolus. When administered in the water, the dose may actually vary among animals, depending on their water intake.

## Regulatory Information

Cattle and pig withdrawal times: 5 days for meat with the oral powder; 18 days for meat and 72 hours for milk when used as intrauterine bolus in cattle; and 12, 14, and 24 days when oral tablets are used for intrauterine treatment, depending on product (check label of individual products).

## Thenium Closylate

thee'nee-um klo'e'sill-ate

**Trade and other names:** Canopar

**Functional classification:** Antiparasitic

## Pharmacology and Mechanism of Action

Antiparasitic drug. Thenium is an antiparasitic drug with action specific for hookworms.

## Indications and Clinical Uses

Thenium closylate is used to treat adult forms of the species *Ancylostoma caninum* and *Uncinaria stenocephala* (hookworms).

### Precautionary Information

#### Adverse Reactions and Side Effects

Thenium may cause occasional vomiting after oral administration.

#### Contraindications and Precautions

No contraindications are reported for animals.

#### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

Tablet is bitter if coating is broken.

## Patient Monitoring and Laboratory Tests

Monitor fecal samples for evidence of parasites.

### Formulations

- Thenium closylate is available in 500-mg tablets (veterinary preparation).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

- Dogs weighing >4.5 kg: 500 mg PO once and repeat in 2-3 weeks.
- Dogs weighing 2.5-4.5 kg: 250 mg (one-half tablet) twice a day PO for 1 day; repeat in 2-3 weeks.

### Large Animal Dosage

- No doses have been reported for large animals.

### Regulatory Information

Do not administer to animals intended for food.

## Theophylline

thee-off'ih-lin

**Trade and other names:** Many generic brands and theophylline sustained release.

**Functional classification:** Bronchodilator

### Pharmacology and Mechanism of Action

Methylxanthine bronchodilator. Nonselective phosphodiesterase (PDE) inhibitor. Phosphodiesterase is the enzyme that converts cyclic adenosine monophosphate (cAMP) to inactive forms. Therapeutic effects may be caused by cAMP or antagonism of adenosine. There appears to be both anti-inflammatory action and bronchodilating action. Sustained-release preparations are used to decrease frequency of administration. Oral theophylline is well absorbed orally in dogs, cats, and horses with bioavailability exceeding 90%. After absorption, theophylline has a half-life in dogs, cats, and horses of 5-6 hours, 14-18 hours, and 12-15 hours, respectively. Some oral formulations contain aminophylline, and theophylline is the active component of aminophylline.

### Indications and Clinical Uses

Theophylline is administered for inflammatory airway disease in cats, dogs, and horses. Use in animals has been primarily derived from empirical use, some experimental models, and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. It has been used to control clinical signs of reversible airway constriction, such as seen with feline asthma. In dogs, the uses include collapsing trachea, bronchitis, and other airway diseases. In horses, it will relieve signs of RAO (heaves), but the IV dose may cause adverse effects in horses. Other drugs (e.g., clenbuterol, albuterol) are often used for this condition in horses. It has not been effective for respiratory diseases in cattle. In dogs and cats, human-labeled extended-release tablets and capsules may be used twice daily in dogs and once daily in cats to achieve effective blood concentrations.

Other methylxanthine drugs have been examined for treatment of dogs and cats with airway disease, but these medications are not readily available in the US or widely used. These drugs include propentofylline, which is an approved veterinary drug in some countries (Karsivan or Vivitonin), as 50-mg tablets for dogs administered at a dose of 3-5 mg/kg q12h PO (cat dose: 5 mg/kg). It has been effective for

feline bronchial disease. In dogs it is approved for treatment of cognitive dysfunction in aged dogs (lethargy, apathy, stiff gait, poor appetite, etc.).

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Adverse effects of theophylline include nausea, vomiting, and diarrhea. With high doses, tachycardia, excitement, tremors, and seizures are possible. Cardiovascular and central nervous system (CNS) adverse effects appear to be less frequent in dogs than people. Overdoses can cause hypokalemia.

#### **Contraindications and Precautions**

Administer with caution to patients with cardiovascular disease or patients with seizure disorders. Studies in people have concluded that administration of methylxanthines increases risk of seizures in susceptible patients.

#### **Drug Interactions**

Use cautiously with other PDE inhibitors such as pentoxifylline, sildenafil (Viagra), and pimobendan. Many drugs will inhibit the metabolism of theophylline and potentially increase concentrations. Drugs responsible include cimetidine, erythromycin, fluoroquinolones, and propranolol. Some drugs will decrease concentrations by increasing metabolism. Such drugs include phenobarbital and rifampin.

### **Instructions for Use**

Adjust dose to maintain therapeutic blood levels. Older slow-release and extended-release formulations are no longer available. Pharmacokinetic studies have established doses for human-labeled tablets and capsules in dogs and cats. These formulations have produced the most consistent plasma concentrations from oral dosing.

### **Patient Monitoring and Laboratory Tests**

Plasma concentrations of theophylline should be monitored in patients receiving chronic therapy to maintain plasma concentrations between 10 and 20 mcg/mL. Regularly monitor plasma concentrations in patients receiving chronic treatment. Peak-trough concentration measurements are encouraged.

### **Formulations**

- Theophylline is available in 100-, 125-, 200-, 250-, and 300-mg tablets; 27-mg/5-mL (5.3-mg/mL) oral solution or elixir; and injection in 5% dextrose. Theophylline extended release is available in 100-, 200-, 300-, 400-, 450-, and 600-mg tablets. However, availability of various sizes of extended-release formulations may vary.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Theophylline is slightly soluble in water (8 mg/mL). It has been mixed with some oral liquids and found to be stable if administered shortly after mixing. When using the slow-release tablets or capsules in dogs and cats, do not disrupt coating on formulation.

### **Small Animal Dosage**

#### **Dogs**

- Theophylline: 9 mg/kg q6-8h PO (immediate-release formulations)
- Theophylline sustained release: 10 mg/kg q12h PO.

#### **Cats**

- 4 mg/kg q8-12h PO (immediate-release formulations).

- Theophylline sustained release: 20 mg/kg for tablets (100 mg per cat) q24h PO or 25 mg/kg for extended-release capsule (125 mg per cat) q24h PO. With long-term use in cats, this interval may be increased to q48h.

### Large Animal Dose

- Horses, treatment of RAO: 5 mg/kg q12h PO.
- Although theophylline has been administered to horses intravenously, this administration has caused transient excitement and restlessness. Give IV administration slowly.
- Cattle use as a bronchodilator: 20 mg/kg q12h PO. When treating diseases secondary to virus infections, decrease frequency to once every 24 hours.

### Regulatory Information

Withdrawal times are not established. However, for extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 3

## Thiabendazole

thye-ah-ben'dah-zole

**Trade and other names:** Omnizole, Equizole, TBZ, and Thibenzole

**Functional classification:** Antiparasitic

### Pharmacology and Mechanism of Action

Benzimidazole antiparasitic drug. Like other benzimidazoles, it produces a degeneration of the parasite microtubule and irreversibly blocks glucose uptake in parasites. Inhibition of glucose uptake causes depletion of energy stores in the parasite, eventually resulting in death. However, there is no effect on glucose metabolism in mammals.

### Indications and Clinical Uses

Availability of commercial forms of thiabendazole has been limited. In horses, it has been used for control of large and small strongyles; *Strongyloides*, and pinworms of the genera *Strongylus*, *Cyathostomum*, and *Cylicobrachytus* and related genera *Cra-terostomum*, *Oesophagodontus*, *Poteriostomum*, and *Oxyuris*. In ruminants, it has been used for infections of GI roundworms in sheep and goats (*Trichostrongylus* spp., *Haemonchus* spp., *Ostertagia* spp., *Cooperia* spp., *Nematodirus* spp., *Bunostomom* spp., *Strongyloides* spp., *Chabertia* spp., *Oesophagostomum* spp., *Trichostrongylus colubriformis* and *T. axei*, and *Ostertagia* spp.).

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are uncommon.

#### Contraindications and Precautions

No contraindications are reported for animals.

#### Drug Interactions

No drug interactions have been reported in animals.



**Instructions for Use**

Thiabendazole is ordinarily administered to horses and cattle. Experience in small animals is limited.

**Patient Monitoring and Laboratory Tests**

Monitor fecal samples for evidence of intestinal parasites.

**Formulations Available**

- Thiabendazole is available in paste, pellets, and solution for oral administration and premix for feeds. Some formulations are no longer commercially available.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs**

- 50 mg/kg q24h for 3 days; repeat in 1 month.
- Treating respiratory parasites: 30-70 mg/kg q12h PO.

**Cats**

- *Strongyloides* spp: 125 mg/kg q24h for 3 days.

**Large Animal Dosage****Horses**

- 44 mg/kg PO (single dose).

**Sheep and Goats**

- 44 mg/kg PO (single dose) up to 67 mg/kg PO for some infections.

**Cattle**

- 67 mg/kg PO (single dose) up to 111 mg/kg PO for more severe infections.

**Pigs (Baby Pigs)**

- 67-90 mg/kg PO.

**Regulatory Information**

Withdrawal time for milk: 96 hours.

Sheep and goat withdrawal time for meat: 30 days.

Cattle withdrawal time for meat: 3 days.

Pig withdrawal time for meat: 30 days.

**Thiacetarsemide Sodium**

thye-ass-et-ars'ah-mide soe-dee-um

**Trade and other names:** Caparsolate

**Functional classification:** Antiparasitic

**Note:** Thiacetarsemide sodium is no longer recommended or available for treating heartworm infections in dogs and cats. Melarsomine dihydrochloride (Immiticide) is recommended instead for treatment of adult heartworms. The information on pharmacology and clinical use of thiacetarsemide is listed briefly here for countries where it may still be available and used for treating heartworm infections.

## Pharmacology and Mechanism of Action

Organic arsenical that produces toxicity in parasites such as adult heartworms.

## Indications and Clinical Uses

Thiacetarsemide is used for treatment of adult heartworm infections. Caparsolate is no longer recommended as an adulticide heartworm treatment by the American Heartworm Society. Caparsolate is less effective in cats than in dogs, with a higher incidence of adverse reactions. In dogs, melarsomine is considered safer and has replaced thiacetarsemide for routine treatment.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are common, especially anorexia, vomiting, and hepatic injury. Pulmonary thromboembolism may occur as a consequence of heartworm kill.

#### Contraindications and Precautions

Its use is not recommended in cats unless they can be carefully monitored. Cats are less susceptible to arsenical toxicity than dogs, but they are more prone to pulmonary thromboembolism. If cats are treated, they should be confined under close observation for 3-4 weeks.

#### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

Thiacetarsemide is administered via four injections over 2 days; however, if severe adverse effects are observed, discontinue regimen. Extravasation can result in skin slough. It is recommended to substitute melarsomine for thiacetarsemide, if possible, for treating heartworm disease.

## Patient Monitoring and Laboratory Tests

Monitor renal and hepatic function.

## Formulations

- Thiacetarsemide is available in 10-mg/mL injections. There are no longer commercial supplies of thiacetarsemide, and its availability is uncertain.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 2.2 mg/kg IV twice daily for 2 days.

### Cats

- Not recommended, unless the cat can be closely supervised. Dose is 2.2 mg/kg twice daily IV for 2 consecutive days.

## Large Animal Dosage

- No doses have been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

## Thiamine Hydrochloride

thye'ah-min hye-droe-klor'ide

**Trade and other names:** Vitamin B<sub>1</sub>, Bewon, and generic brands

**Functional classification:** Vitamin

### Pharmacology and Mechanism of Action

Vitamin B<sub>1</sub> is used for treatment of vitamin deficiency. Vitamin B complex often contains thiamine (B<sub>1</sub>), riboflavin, niacinamide, and cyanocobalamin B<sub>12</sub>.

### Indications and Clinical Uses

Thiamine is used to provide vitamin B<sub>1</sub> supplementation or to treat vitamin B<sub>1</sub> deficiency.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are rare because water-soluble vitamins are easily excreted.

#### Contraindications and Precautions

Administer solutions of vitamin B<sub>1</sub> very slowly intravenously, if at all. Rapid IV administration has caused anaphylactic reactions.

#### Drug Interactions

Thiamine hydrochloride may be susceptible in incompatibility when this hydrochloride is mixed with alkalinizing solutions.

### Instructions for Use

Vitamin B supplements are administered often in combination with other B vitamins as vitamin B complex solutions.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Thiamine is available in 250-mcg/5-mL elixir, 5- to 500-mg tablets, and 100- and 500-mg/mL injections.
- Vitamin B complex aqueous solutions for injection usually contain 12.5 mg/mL of vitamin B<sub>1</sub>.

### Stability and Storage

Store in a tightly sealed container, at room temperature, and protected from light. When mixed with other solutions (e.g., fluid solutions), incompatibility may result.

### Small Animal Dosage

#### Dogs

- 10-100 mg/dog/day PO.
- 12.5-50 mg/dog/day IM or SQ.

#### Cats

- 5-30 mg/cat/day PO up to a maximum dose of 50 mg/cat/day.
- 12.5-25 mg/cat/day IM or SQ.

### Large Animal Dosage

- All doses are listed on a per-animal basis.

#### Lambs

- 12.5-25 mg/day IM.

#### Sheep and Pigs

- 65-125 mg/day IM.

#### Calves and Foals

- 37.5-65 mg/day IM.

#### Cattle and Horses

- 125-250 mg/day IM.

### Regulatory Information

Withdrawal time for animals intended for food: 0 days.

## Thioguanine

thye-oh-gwah'neen

**Trade and other names:** Generic brands

**Functional classification:** Anticancer agent

### Pharmacology and Mechanism of Action

Anticancer agent. Antimetabolite of purine analogue type. Thioguanine inhibits DNA synthesis in cancer cells.

### Indications and Clinical Uses

Thioguanine is used in some anticancer protocols. It is not commonly used in animals. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects, as with any anticancer drug, are expected. Adverse effects from thioguanine may be similar to those observed from mercaptopurine. Immunosuppression and leukopenia are common.

#### Contraindications and Precautions

Do not administer to patients with depressed bone marrow.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Thioguanine may be combined with other agents for treatment of cancer.

### Patient Monitoring and Laboratory Tests

Monitor complete blood count (CBC) to screen for evidence of bone marrow toxicity.

### Formulations

- Thioguanine is available in 40-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs**

- 40 mg/m<sup>2</sup> q24h PO.

**Cats**

- 25 mg/m<sup>2</sup> q24h PO for 1-5 days, then repeat every 30 days.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

**Thiopental Sodium**

thye-oh-pen'tahl soe'dee-um

**Trade and other names:** Pentothal, previously used name was Thiopentone.

**Functional classification:** Anesthetic, barbiturate

**Pharmacology and Mechanism of Action**

Ultrashort-acting barbiturate. Anesthesia is produced by CNS depression without analgesia. The action of thiopental is similar to other barbiturates. It is a gamma-aminobutyric acid (GABAA) receptor agonist which enhance inhibitory neurotransmission. It increases GABA binding (inhibitory neurotransmitter) to its receptor, which increases transmembrane chloride conductance resulting in hyperpolarization of the postsynaptic cell membrane and inhibition of the postsynaptic neuron. Anesthesia is terminated by redistribution in the body.

**Indications and Clinical Uses**

Thiopental is the most commonly used injectable barbiturate in veterinary medicine. It is used primarily for induction of anesthesia or for short duration of anesthesia (10- to 15-minute procedures). It induces a rapid, smooth, and generally excitement-free induction. It can be administered intravenously, with prior premedication of other anesthetic adjuncts such as tranquilizers and sedatives (e.g., alpha<sub>2</sub>-agonists, phenothiazines, and opiates).

**Precautionary Information****Adverse Reactions and Side Effects**

The most common effect is transient apnea and respiratory depression. Other adverse effects are related to the anesthetic effects of the drug. Thiopental may cause cardiovascular depression with a slight decrease in stroke volume and little change in cardiac output or blood pressure. Premedication will reduce the risk of cardiovascular events. Supplementation with oxygen during induction also will decrease cardiovascular events. Overdoses are caused by rapid or repeated injections. Avoid extravasation outside of the vein.

### Contraindications and Precautions

Use carefully in patients with respiratory or cardiac disease. Do not use unless there is an ability to monitor and maintain respiration.

### Drug Interactions

Thiopental is compatible with other anesthetics. However, use of other sedatives and anesthetics will lower dose of thiopental. Thiopental has been combined with propofol in a 1:1 mixture without loss of effectiveness. This mixture of 1:1 2.5% thiopental and propofol has been used to induce anesthesia in dogs.

### Instructions for Use

Therapeutic index is low. Use only in patients in which it is possible to monitor cardiovascular and respiratory functions. Thiopental is often administered with other anesthetic adjuncts.

### Patient Monitoring and Laboratory Tests

Monitor cardiovascular and respiratory function during anesthesia with thiopental.

### Formulations

- Thiopental is available in 250-mg to 10-g vials (mix to desired concentration with sterile diluent). The concentration can vary, but generally the 2.5% solution is used with small animals and the 2.5% or 5% solution used with larger animals.

### Stability and Storage

Thiopental, when prepared properly, is chemically stable and resists bacterial growth for up to 4 weeks when refrigerated. Thiopental has a pH of 10-11 and should not be mixed with acidifying solutions. If mixed with other drugs, the alkalinity may affect their stability. Propofol has been mixed with thiopental sodium in a 1:1 mixture, and they are physically and chemically compatible if used promptly.

### Small Animal Dosage

#### Dogs

- 10-25 mg/kg IV (to effect).

#### Cats

- 5-10 mg/kg IV (to effect).

### Large Animal Dosage

#### Cattle

- Induction: 6-12 mg/kg IV (to effect).

#### Pigs

- 10-20 mg/kg IV (to effect).

### Regulatory Information

Extralabel use: Establish a withdrawal time of at least 1 day for meat and 24 hours for milk. Pig withdrawal time for meat: 0 days.

Schedule III controlled drug.

RCI Classification: 2

## Thiotepa

thye-oh-tep'ah

**Trade and other names:** Thioplex and generic brands

**Functional classification:** Anticancer agent

### Pharmacology and Mechanism of Action

Anticancer agent. Thiotepa is an alkylating agent of the nitrogen mustard type (similar to cyclophosphamide).

**Indications and Clinical Uses**

Thiotepa is used for various tumors, especially malignant effusions. The most common mode of administration is in a lesion or locally (e.g., in a bladder). For cancer of the bladder, 30 mg is diluted in 30 mL of distilled water and instilled directly in the bladder once per week.

**Precautionary Information****Adverse Reactions and Side Effects**

Adverse effects are similar to other anticancer agents and alkylating drugs (many of which are unavoidable). Bone marrow suppression is the most common effect.

**Contraindications and Precautions**

Avoid use in animals with depressed bone marrow.

**Drug Interactions**

No drug interactions have been reported in animals.

**Instructions for Use**

One should consult the specific cancer chemotherapy protocol for guidance on administration. Thiotepa usually is administered directly in body cavities.

**Patient Monitoring and Laboratory Tests**

Monitor CBC for evidence of bone marrow suppression.

**Formulations**

Thiotepa is available in 15-mg injections (usually in a solution of 10 mg/mL).

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. When mixing solution, add 1.5 mL of sterile water to each vial. This solution is stable for 5 days if refrigerated. Solutions may be clear to slightly opaque, but if cloudiness or precipitate appears, discard vial.

**Small Animal Dosage****Dogs and Cats**

- 0.2-0.5 mg/m<sup>2</sup> weekly or daily for 5-10 days IM, intracavitary, or intratumor.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

**Thyroid-Releasing Hormone**

**Trade and other names:** TRH, Protirelin, Thyrel

**Functional classification:** Hormone, thyroid

**Pharmacology and Mechanism of Action**

Thyroid-releasing hormone (TRH) is used to detect hyperthyroidism when T<sub>4</sub> is not elevated, yet hyperthyroidism is suspected. It is a synthetic tripeptide that is believed

to be structurally identical to the naturally occurring thyrotropin-releasing hormone produced by the hypothalamus.

### Indications and Clinical Uses

Thyroid-releasing hormone has been used for diagnostic testing. See [thyrotropin](#) (TSH) for diagnostic testing for hypothyroidism. There are no specific therapeutic uses.

### Precautionary Information

#### Adverse Reactions and Side Effects

No significant adverse effects have been reported. Allergic reactions are possible.

#### Contraindications and Precautions

No contraindications are reported for animals.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Used for diagnostic purposes.

### Patient Monitoring and Laboratory Tests

Monitor thyroid concentrations. Collect post-TRH  $T_4$  sample at 4 hours after test dose.

### Formulations

- Thyrel TRH (Protirelin) is supplied as 1-mL ampules. Each ampule contains 500  $\mu$ g protirelin, but is currently difficult to obtain.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

- Collect baseline  $T_4$ , followed by 0.1 mg/kg IV. Collect post-TRH  $T_4$  sample at 4 hours.

### Large Animal Dosage

- To test for pituitary pars intermedia dysfunction (PPID) in horses (equine Cushing syndrome), administer 1 mg synthetic TRH IV and collect samples. Optimum sample time is 0 and 30 minutes.

### Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Thyrotropin

thye-roe-troe'pin

**Trade and other names:** Thytropar, Thyrogen, and TSH

**Functional classification:** Hormone, thyroid

### Pharmacology and Mechanism of Action

Thyroid-stimulating hormone is used for diagnostic testing; it stimulates normal secretion of thyroid hormone. The formulations available include Thyrogen (thyrotropin alpha for injection), which is a purified recombinant form of human TSH produced by recombinant DNA technology. An older form, Thytropar, is difficult to obtain.



## 782 Thyrotropin

The amino acid sequence of thyrotropin alpha is identical to that of human pituitary TSH. Thyroid-stimulating hormone activity is not species specific, and the human product may be used in animals.

Recombinant human thyrotropin (rhTSH) has been used for the diagnosis of hypothyroidism.

### Indications and Clinical Uses

Thyroid-stimulating hormone is used to stimulate secretion of thyroid hormone for diagnostic testing. Because of the limited availability of TSH for diagnostic testing and the high cost of the human form, this test is rarely performed. Bovine TSH (bTSH) has been used in dogs, but anaphylactoid reactions and safety concerns led to a discontinuation of the use. Human recombinant thyrotropin (rhTSH) can be administered IV and results in a total  $T_4$  (TT4) increase at 4 and 6 hours.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse reactions are rare. In people, allergic reactions have occurred.

#### Contraindications and Precautions

No contraindications have been reported for animals.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

To prepare solution, add 2 mL sodium chloride to a 10-unit vial. Consult testing laboratory for specific guidelines for thyroid testing.

If the patient is already receiving thyroxine supplement, withdraw treatment for 6-8 weeks before testing.

### Patient Monitoring and Laboratory Tests

After IV injection, collect post-TSH sample at 4 or 6 hours (6 hours is optimal). See [dosing](#) section for complete information on testing in dogs.

### Formulations

- Recombinant human TSH, also known as thyrotropin alpha or Thyrogen, is available in a 1.1-mg vial containing thyrotropin alpha. After reconstitution with 1.2 mL of sterile water, the thyrotropin alpha concentration is 0.9 mg/mL (see [dose](#) section for specific instructions for preparing canine dose). The pH of the reconstituted solution is approximately 7.0. Other forms (Thytropar) are difficult to obtain. Bovine TSH caused reactions in dogs and is no longer available.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Reconstituted solutions retain potency for 2 weeks at 2° C-8° C, for 4 weeks at 4° C, and 12 weeks if frozen (-20° C).

### Small Animal Dosage

#### Dogs

- 50-150 mcg injection per dog.
- Diagnostic testing for dogs: Reconstitute 1 vial (1.1 mg) with 6 mL sterile water and divide into 12 aliquots. Place 0.5 mL in plastic insulin syringes and store in freezer. For each dose, thaw syringe and administer IV one syringe per dog. The dose used has ranged from 75 mcg per dog to 150 mcg per dog. The higher dose is reported

to have better discriminating power. After injection, measure thyroid hormone ( $T_4$ ) at 4 or 6 hours after injection (6 hours is optimal). Post-TSH response should be at least 1.9 mcg/dL over baseline. Generally, a response of 2.5-3.1 mcg/dL is consistent with euthyroidism; < 1.6 mcg/dL is indicative of hypothyroidism; and, 1.6-2.5 mcg/mL is in the intermediate range and may require follow-up testing.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Ticarcillin Disodium

tye-kar-sill'in dye-soe-dee-um

**Trade and other names:** Ticar and Ticillin

**Functional classification:** Antibacterial

**Note:** The formulations of ticarcillin have been withdrawn from the human market, as well as formulations containing clavulanate. There is still an approved veterinary formulation for horses, but availability may be limited.

### Pharmacology and Mechanism of Action

Beta-lactam antibiotic. Like other beta lactams, ticarcillin binds penicillin-binding proteins (PBPs) that weaken or interfere with cell wall formation. After binding to PBPs, the cell wall weakens or undergoes lysis. Like other beta-lactams, this drug acts in a time-dependent manner, which indicates that it is more effective when drug concentrations are maintained above the MIC values during the dose interval. Ticarcillin has action similar to ampicillin/amoxicillin and a spectrum similar to carbenicillin. It is primarily used for gram-negative infections, especially those caused by *Pseudomonas* spp.

### Indications and Clinical Uses

Ticarcillin has been used in animals for treatment of various infections, including pneumonia, soft tissue infections, and bone infections. It has similar activity as ampicillin, but is extended to include many organisms that otherwise are resistant to ampicillin, such as *Pseudomonas aeruginosa* and other gram-negative bacilli. Its activity is enhanced when administered with an aminoglycoside. Use in animals has been primarily derived from empirical use and from pharmacokinetic-pharmacodynamic information. It is administered intravenously in most animals; IM administration can be painful. Ticarcillin also has been infused in the uterus of horses to treat metritis.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are uncommon. However, allergic reactions are possible. High doses can produce seizures and decreased platelet function.

#### Contraindications and Precautions

Administer cautiously, if at all, to animals with penicillin allergies.

#### Drug Interactions

Do not combine in same syringe or in vial with aminoglycosides.

**Instructions for Use**

Ticarcillin may be combined with clavulanic acid (see [ticarcillin + clavulanate](#) for more details). Ticarcillin is synergistic with, and often combined with, aminoglycosides (e.g., amikacin and gentamicin). Lidocaine (1%) may be used for reconstitution to decrease pain from IM injection (see “[Formulations](#)” section).

**Patient Monitoring and Laboratory Tests**

Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 64$  mcg/mL for *Pseudomonas* and  $\leq 16$  mcg/mL for gram-negative enteric organisms.

**Formulations**

- **Note:** availability of commercial formulations may be limited. Ticarcillin has been available in 3-g vials. Mix 3-g vial with 6 mL sterile water, sodium chloride, or 1% lidocaine hydrochloride solution (without epinephrine) to produce a final concentration of 384.6 mg/mL. Ticarcillin + clavulanate also has been used, but commercial forms have been voluntarily withdrawn from the market (see next section for more information).

**Stability and Storage**

Store powder for injection in original vial, protected from light, and at room temperature. Use reconstituted solution immediately. If diluted for IV administration with sodium chloride or 5% dextrose, it may be stable for up to 72 hours at room temperature or 14 days if refrigerated. Intravenous solution prepared in lactated Ringer's solution is stable for up to 48 hours at room temperature or 14 days if refrigerated. If diluted IV solutions are frozen, they are stable for up to 30 days but should be used within 24 hours once thawed. Do not refreeze thawed solutions.

**Small Animal Dosage****Dogs and Cats**

- 33-50 mg/kg q4-6h IV or IM.

**Large Animal Dosage****Horses**

- 44 mg/kg q6-8h IV or IM.
- Ticarcillin also has been used in horses as an intrauterine infusion at a dose of 12.4 mg/kg diluted in 60-100 mL saline.

**Regulatory Information**

Withdrawal times are not established. However, excretion is similar to other beta-lactam antibiotics, such as ampicillin. Follow ampicillin guidelines for withdrawal times.

**Ticarcillin + Clavulanate Potassium**

tye-kar-sill'in + klav'yoo-lan'ate

**Trade and other names:** Timentin

**Functional classification:** Antibacterial

**Note:**

The manufacturer has voluntarily withdrawn ticarcillin + clavulanate from the market in the US. It is an FDA-approved product, but no longer marketed. Information is included regarding pharmacology, indications, and dosing in the event that it returns to the market in the future. If another injectable penicillin beta-lactamase inhibitor is

indicated in a patient, the combination of piperacillin and tazobactam is a logical substitute. Consult the section on piperacillin and tazobactam for more information on the pharmacology and clinical use.

### Pharmacology and Mechanism of Action

Action and spectrum are the same as ticarcillin, except clavulanic acid has been added to inhibit bacterial beta-lactamase and increase spectrum of activity. However, clavulanate does not increase activity against *Pseudomonas* compared to ticarcillin alone.

### Indications and Clinical Uses

Ticarcillin + clavulanate has been used in animals for treatment of various infections, including pneumonia, soft tissue infections, and bone infections. Ticarcillin has similar activity as ampicillin, but is extended to include many organisms that otherwise are resistant to ampicillin, such as *Pseudomonas aeruginosa* and other gram-negative bacilli. When combined with clavulanate, the activity against some strains of gram-negative bacteria and *Staphylococcus* is improved. However, methicillin-resistant staphylococci are resistant to ticarcillin. Its activity against *P. aeruginosa* may be enhanced when administered with an aminoglycoside. Use in animals has been primarily derived from empirical use and pharmacokinetic–pharmacodynamic information. It is administered intravenously in most animals; IM administration can be painful.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are uncommon. However, allergic reactions are possible. High doses can produce seizures and decreased platelet function.

#### Contraindications and Precautions

Administer cautiously, if at all, to animals with penicillin allergies.

#### Drug Interactions

Do not combine in same syringe or in vial with aminoglycosides.

### Instructions for Use

Ticarcillin is synergistic with, and often combined with, aminoglycosides (e.g., amikacin and gentamicin). Lidocaine (1%) may be used for reconstitution to decrease pain from IM injection.

### Patient Monitoring and Laboratory Tests

Susceptibility testing: CLSI break point for sensitive organisms is  $\leq 64/2$  mcg/mL for *Pseudomonas* and  $\leq 16/2$  mcg/mL for gram-negative bacilli. (The “/” distinguishes the ticarcillin from the clavulanate concentrations.)

### Formulations Available

- Note: Recently the formulations of this product have become commercially unavailable. Ticarcillin + clavulanate was ordinarily available in 3-g/vial injections. Each 3-g vial contains ticarcillin (as disodium) and 0.1 g clavulanic acid (as potassium). It also contains 4.75 mEq sodium and 0.15 mEq potassium per gram.

### Stability and Storage

Store in original vial and at room temperature. The reconstituted solution is stable for up to 6 hours at room temperature or 72 hours if refrigerated. The IV diluted solution (10–100 mg/mL) prepared with lactated Ringer's or sodium chloride is stable for up to 24 hours at room temperature, up to 4 days if refrigerated, or 30 days if frozen. The IV solution diluted to 10–100 mg/mL with 5% dextrose may be stored for up to 24 hours at room temperature, up to 3 days if refrigerated, or 7 days if

frozen. When using frozen solutions, thaw at room temperature or in refrigerator, but do not speed thawing by using immersion in water baths or by microwave. The thawed solution is stable for 24 hours at room temperature or 7 days if refrigerated. Do not refreeze thawed solutions.

### Small Animal Dosage

#### Dogs and Cats

- Dose according to rate for ticarcillin: 33-50 mg/kg q4-6h IV or IM.

### Large Animal Dosage

#### Horses

- 44 mg/kg q6-8h IV or IM (of the ticarcillin component).
- Ticarcillin + clavulanate also has been used in horses as an intrauterine infusion at a dose of 12.4 mg/kg ticarcillin and 0.4 mg/kg clavulanate diluted in 60-100 mL saline.

### Regulatory Information

Withdrawal times are not established. However, excretion is similar to other beta-lactam antibiotics, such as ampicillin. Follow ampicillin guidelines for withdrawal times.

## Tildipirosin

Til'-di-pir'-oh-sin

**Trade and other names:** Zuprevo

**Functional classification:** Antibacterial, Macrolide

### Pharmacology and Mechanism of Action

Tildipirosin is an antibacterial of the macrolide class. It is a 16-membered ring (tilmicosin also is a 16-member ring molecule) macrolide antimicrobial with three charged nitrogen atoms (tulathromycin also has 3 charged nitrogen atoms). Like other macrolides, it inhibits bacterial protein synthesis by binding to the ribosomal 50S subunit, specifically, the 23S rRNA within the 50S subunit. After binding, tildipirosin interacts with ribosomal RNA (rRNA) and ribosomal proteins adjacent to the peptidyl-transferase enzyme. Thus like other macrolides, it inhibits protein synthesis by blocking the prolongation and release of developing polypeptides. Tildipirosin has a spectrum of activity that is limited to gram-positive bacteria and some gram-negative bacteria that cause respiratory diseases in cattle and pigs (e.g., *Mannheimia haemolytica*, *Mycoplasma*, *Pasteurella multocida*, *Actinobacillus pleuropneumoniae*, *Bordetella bronchiseptica*, and *Haemophilus parasuis*). *Escherichia coli* and *Pseudomonas aeruginosa* are resistant. Some *Staphylococcus* spp. and *Streptococcus* spp. may be susceptible.

There is evidence for bactericidal activity against *M. haemolytica*, bovine *P. multocida*, *Histophilus somni*, *H. parasuis*, and *Actinobacillus pleuropneumoniae* and bacteriostatic activity against *B. bronchiseptica*.

Pharmacokinetics in cattle shows that the half-life is long (mean 204 hours, or 8.5 day plasma half-life), with a peak concentration at the label dose of 0.64 mcg/mL and bioavailability from injection in cattle of 79%. The volume of distribution, like most macrolide antibiotics, is large, with a volume of distribution in cattle of 49 L/kg. The lung concentrations in cattle are over 150 times the plasma drug

concentrations with a half-life of 10 days. Bronchial fluid concentrations are approximately 40 times the plasma drug concentrations, with a half-life of 11 days.

In pigs, the plasma half-life is 106 hours (4.4 days), with a peak concentration of 0.9 mcg/mL after IM injection of 4 mg/kg. The lung concentrations in pigs were approximately 80 times higher than plasma concentrations with a half-life of 6.8 days. The bronchial fluid concentrations were 680 times higher than plasma drug concentrations at 5 days after injection.

Tildipirosin, like other macrolides, exerts therapeutic benefits not solely explainable by antibacterial activity. Like azithromycin, tildipirosin may have multiple immunomodulatory effects that likely contribute to the therapeutic response in respiratory infections, and perhaps other diseases. Other beneficial effects may be caused by enhanced degranulation and apoptosis of neutrophils and inhibition of inflammatory cytokine production. It also may help clear infections by enhancing macrophage functions.

### Indications and Clinical Uses

Tildipirosin has been approved for the treatment and control/prevention of cattle with BRD associated with *M. haemolytica*, *P. multocida* and *H. somni* and in some European countries for the treatment of pigs with SRD associated with *A. pleuropneumoniae*, *P. multocida*, *B. bronchiseptica*, and *H. parasuis*. The use in other animals for treatment of respiratory disease has not been reported.

Other long-acting macrolide antibiotics used in cattle include tilmicosin, tulathromycin, and gamithromycin.

### Precautionary Information

#### Adverse Reactions and Side Effects

Serious systemic adverse reactions have not been observed. In cattle, tildipirosin injection may cause injection site swelling and inflammation that may be severe. Swelling and visible lesions in edible tissue can persist at least 35 days after injection.

Because of structural similarities between tildipirosin and tilmicosin (both are 16-membered macrolides), cardiotoxic studies were performed in dogs. At 10 mg/kg IM, there was no effect, and at 20 mg/kg there were changes in pulse pressure. In an oral dose study in dogs, there were no electrocardiogram (ECG) changes following single (300 mg/kg body weight) or repeated (150 or 200 mg/kg daily for two days and 200 mg/kg daily for seven days) doses.

#### Contraindications and Precautions

Except for regulatory restrictions (see below), no specific contraindications have been reported.

#### Drug Interactions

No drug interactions have been reported. Macrolide antibiotics may interfere with cytochrome P450 enzyme activity, but this has not been studied for tildipirosin. Antibacterial activity is decreased in an acidic environment.

### Instructions for Use

In cattle, administer as a single SQ injection in the neck. Do not inject more than 10 mL per injection site. In pigs (in countries where approved) administer as a single IM injection.

### Patient Monitoring and Laboratory Tests

CLSI break point for susceptibility is  $\leq 4.0$  mcg/mL.

**Formulations**

Tildipirosin is available in a 180-mg/mL (18%) solution for injection for cattle and in some European countries, 40-mg/mL solution for injection for pigs.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage**

- No small animal doses have been established.

**Large Animal Dosage****Cattle**

- 4 mg/kg (equivalent to 1 mL/100 pounds) SQ (neck) as a single injection.

**Pigs**

- 4 mg/kg (equivalent to 1 mL/10 kg) IM as a single injection.

**Horses**

- No dosing information is available for horses.

**Regulatory Information**

No milk withdrawal times are established. Do not use in female dairy cattle 20 months of age or older. Do not use in veal calves.

Cattle withdrawal time for meat: 21 days.

Pig withdrawal time for meat: 7 days.

**Tiletamine and Zolazepam**

till-eh'tah-meen + zole-az'eh-pam

**Trade and other names:** Telazol and Zoletil

**Functional classification:** Anesthetic

**Pharmacology and Mechanism of Action**

Anesthetic. It is a combination of tiletamine (dissociative anesthetic agent similar in action to ketamine) and zolazepam (benzodiazepine similar in action as diazepam). Tiletamine + zolazepam produces a short duration (30 minutes) of anesthesia. In cats, the effect of the zolazepam will have a longer duration than tiletamine. In dogs, the tiletamine will have a longer duration than the zolazepam. Therefore anesthesia appears to be smoother in cats than in dogs.

**Indications and Clinical Uses**

Tiletamine + zolazepam is used for short-term anesthesia in animals. For longer procedures, other drugs should be used.

**Precautionary Information****Adverse Reactions and Side Effects**

Tiletamine + zolazepam has a wide margin of safety, which is greater in cats than in dogs. Side effects include excessive salivation (may be antagonized with atropine), erratic recovery, and muscle twitching. Drying of the cornea may occur unless ophthalmic ointment is applied to the eyes. Adverse reactions have been observed when administered to ferrets.

**Contraindications and Precautions**

Low doses do not provide sufficient anesthesia for surgery. Do not use in patients with pancreatic disease.

**Drug Interactions**

No drug interactions have been reported in animals.

**Instructions for Use**

Administer by deep IM injection.

**Patient Monitoring and Laboratory Tests**

Monitor heart rate and rhythm during anesthesia. Monitor body temperature because of risk of hypothermia.

**Formulations**

- Tiletamine + zolazepam is available in 50 mg of each component per milliliter (100 mg total per milliliter).

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs**

- Initial IM dose is 6.6-10 mg/kg for minor procedures.
- Short-term anesthesia: 10-13 mg/kg IM.

**Cats**

- 10-12 mg/kg IM for minor procedures and higher doses of 14-16 mg/kg IM for surgery.
- Doses are based on combined milligrams of each component.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule III controlled drug

**Tilmicosin Phosphate**

til-mye'koe-sin foss'fate

**Trade and other names:** Micotil and Pulmotil AC (for water), Pulmotil tilmicosin premix

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Macrolide antibiotic. Tilmicosin is a 16-membered macrolide structure (tildipirosin is also a 16-member macrolide) with two charged nitrogen atoms. Like other macrolides, it inhibits bacterial protein synthesis by binding to the ribosomal 50S subunit, specifically, the 23S rRNA within the 50S subunit. After binding, tildipirosin interacts with rRNA and ribosomal proteins adjacent to the peptidyl-transferase enzyme. Thus



like other macrolides, it inhibits protein synthesis by blocking the prolongation and release of developing polypeptides. Tilmicosin has a spectrum of activity that is limited primarily to gram-positive aerobic bacteria; *Mycoplasma*; and respiratory pathogens such as *Pasteurella multocida*, *Mannheimia haemolytica*, and *Histophilus somni* (formerly *Haemophilus somnus*).

In cattle, tilmicosin has a half-life of 28 hours in plasma from IV treatment and 31 hours after SQ treatment. The volume of distribution is 28 L/kg.

Tilmicosin, like other macrolides, exerts therapeutic benefits not solely explainable by antibacterial activity. Anti-inflammatory effects may include some reduced leukocyte release of inflammatory mediators in the lungs associated with tilmicosin treatment. There also may be reduced prostaglandin synthesis with tilmicosin administration in alveolar macrophages. Other beneficial effects may be caused by enhanced degranulation and apoptosis of neutrophils and inhibition of inflammatory cytokine production. It also may help clear infections by enhancing macrophage functions.

### Indications and Clinical Uses

Tilmicosin activity against respiratory pathogens is effective for prevention and treatment of BRD and ovine respiratory disease (ORD) in sheep associated with *M. haemolytica*. One injection has duration of at least 72 hours, based on prolonged half-life. When used to control BRD in calves that are entering feedlots, the use of tilmicosin at the time of feedlot arrival has reduced incidence of respiratory disease in cattle. Tilmicosin can be added to feed of cattle for the control of BRD associated with *M. haemolytica*, *P. multocida*, and *H. somni* in groups of beef and nonlactating dairy cattle where active BRD has been diagnosed in at least 10% of the animals in the group.

Tilmicosin (Pulmotil) is used in medicated feed and water for swine for control of SRD associated with *Actinobacillus pleuropneumoniae*, *P. multocida*, and *Haemophilus parasuis*.

Other long-acting macrolide antibiotics used in cattle include gamithromycin, tildipirosin, and tulathromycin.

### Precautionary Information

#### Adverse Reactions and Side Effects

Tilmicosin may be cardiotoxic in some animals. Injections to pigs have been fatal because of cardiotoxicity. The cardiac effects are increased heart rate and decreased contractility. However, administration of tilmicosin premix in feed of pigs has been safe. In dogs, tilmicosin injections have caused cardiac toxicosis and may be caused by calcium-channel blockade; it was reversed by administration of calcium. In goats, injections greater than 10 mg/kg IM or SQ can cause toxicity. In horses, injections of tilmicosin IM or SQ >10 mg/kg can lead to toxicity. Do not administer intravenously to any species. Treatment of accidental injection in people must be prompt to avoid fatal reactions. Treatment consists of beta-adrenergic agonists (e.g., dobutamine) and supportive care.

#### Contraindications and Precautions

Tilmicosin reaches high concentrations in milk for up to 42 days. Do not administer to lactating dairy cattle. Do not administer to goats. Do not allow horses or other equine access to feeds containing tilmicosin. Do not administer to any animals intravenously or death can result. People handling tilmicosin should take precautions to prevent accidental injection. Fatal cardiac reactions caused by injections have been reported in people. Accidental injection in people requires immediate treatment.

### Drug Interactions

The cardiac adverse effects are exacerbated by administration of beta blockers such as propranolol. Dobutamine and administration of calcium may offset cardiac effects.

### Instructions for Use

Administer SQ. If a person handling the drug is accidentally injected, consult a physician immediately. Severe cardiac toxicity has occurred in some species of animals. Tilmicosin can also be added to feed and drinking water for pigs.

### Patient Monitoring and Laboratory Tests

Susceptibility information: CLSI breakpoint for susceptible organisms is  $\leq 8$  mcg/mL for bovine respiratory pathogens, and  $\leq 16$  mcg/mL for SRD pathogens. Use of break points for other macrolides may identify organisms sensitive or resistant to tilmicosin.

### Formulations

- Tilmicosin is available in 300-mg/mL injection (Micotil) and 200 g/kg (90.7 g/lb) of premix (Pulmotil). For mixing with water for pigs, it is available as 250 mg tilmicosin/mL.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

- It is not recommended for small animals.

### Large Animal Dosage

#### Cattle

- 10 mg/kg SQ single dose. Avoid IV or IM administration.
- Added to feed: 568-757 grams per ton of feed to provide 12.5 mg/kg body weight for 14 days.

#### Sheep

- 10 mg/kg SQ single dose.

#### Goats

- Do not use.

#### Horses

Do not use. Safety not established.

#### Pigs

- Pneumonia: 181-383 grams per ton of feed. Feed only this ration for 21 days, beginning at the time of disease outbreak.
- Drinking water: add 200 mg tilmicosin/L (200 ppm) for 5 consecutive days.

### Regulatory Information

Cattle withdrawal time for meat: 28 days. No withdrawal time established for milk; if injected intrammary to lactating cows, discard milk for a minimum of 82 days.

Pig withdrawal time for meat: 7 days.

Sheep withdrawal time for meat: 28 days.

## Tiludronate Disodium

Til-u-droe' nate dye-soe'dee-um

**Trade and other names:** Tildren (veterinary form), Skelid (human form)

**Functional classification:** Antihypercalcemic

### Pharmacology and Mechanism of Action

Bisphosphonate drug. Drugs in this class also include pamidronate, etidronate, and pyrophosphate. These drugs are characterized by a germinal bisphosphonate bond. Their clinical use resides in their ability to inhibit bone resorption. These drugs decrease bone turnover by inhibiting osteoclast activity, inducing osteoclast apoptosis, retarding bone resorption, and decreasing the rate of osteoporosis. Inhibition of bone resorption is via inhibition of the mevalonate pathway. Bisphosphonates are classified as nitrogen containing and nonnitrogenous based on the structure, with the nitrogen-containing drugs being more potent. Tiludronate is a nonnitrogenase compound. It also may have some anti-inflammatory properties. Tiludronate has a plasma half-life in horses of 3-7 hours, but bone levels may be retained for months.

### Indications and Clinical Uses

Tiludronate is licensed in countries in Europe and approved in the US for treatment of bone pain associated with navicular syndrome in horses. Other bisphosphonate drugs are used in people to treat osteoporosis and treatment of hypercalcemia of malignancy. In horses, tiludronate is used to treat palmar foot pain caused by navicular disease. It also is used to treat distal tarsal osteoarthritis (bone spavin). Like other drugs in this class, it is helpful for managing complications associated with pathologic bone resorption. It also may provide pain relief in patients with pathologic bone disease. Another bisphosphonate is clodronate (Osphos) also approved for treating navicular disease in horses.

Efficacy studies conducted in horses have shown that at a dose of 0.1 mg/kg for 10 days (1.0 mg total dose), it was effective for treatment of navicular disease and distal tarsal osteoarthritis. Beneficial effects for treating chronic lameness are less certain.

### Precautionary Information

#### Adverse Reactions and Side Effects

Reaction to tiludronate has only been reported for horses. After IV infusion, an increase in heart rate and transient hypocalcemia have been observed. Thirty percent to 45% of horses administered tiludronate develop signs of colic after IV administration and should be monitored. However, colic signs that have been observed in horses resolved uneventfully. Neither effect is considered significant. In people, there is some concern that it may result in excessive mineralization and hardening of the bone, which may result in a greater risk of fractures. However, this effect has not been reported for animals. No adverse effects on bone mineral density have been reported.

#### Contraindications and Precautions

Do not use in horses with kidney disease. The manufacturer warns that concurrent administration of NSAIDs with tiludronate may increase risk of kidney injury. Use carefully in conditions associated with hypocalcemia. It is not recommended

to administer bisphosphonates to young growing animals. Do not use in pregnant mares, as the safety in pregnancy has not been evaluated.

### Drug Interactions

Do not mix with solutions containing calcium (e.g., lactated Ringer's solution). Do not administer with NSAIDs (see [precaution](#) earlier). If antacids are used concurrently, magnesium hydroxide and calcium carbonate may reduce effectiveness.

### Instructions for Use

Make sure horses are well hydrated prior to use to avoid kidney injury. For IV infusion, dilute in solvent and infuse slowly over 90 minutes. Observe horses for 4 hours after IV administration for signs of colic.

### Patient Monitoring and Laboratory Tests

Monitor serum calcium and phosphorus. Monitor urea nitrogen, creatinine, urine-specific gravity, and food intake in treated animals.

### Formulations

- Tiludronate is available in 50-mg vials for injection to be reconstituted with 10 mL of diluent.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

- No doses have been established for dogs or cats.

### Large Animal Dosage

#### Horses

- 1 mg/kg administered as 0.1 mg/kg per day for 10 days intravenously or administer as a single 1-mg/kg IV infusion for one dose. Administer IV infusion in 1 L of 0.9% saline solution over 30-60 minutes.

### Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Tinidazole

tih-nih'dah-zole

**Trade and other names:** Tindamax

**Functional classification:** Antiprotozoal

### Pharmacology and Mechanism of Action

Antiprotozoal with action similar to metronidazole. It is a second-generation nitroimidazole in which the activity involves generation of free nitroradicals via metabolism that occurs within protozoa. It has action against *Trichomonas*, *Giardia*, and intestinal protozoal parasites. It also has in vitro activity against anaerobic bacteria and *Helicobacter*. Half-life is approximately 5.5 hours in horses, 8.5 hours in cats, and 4.5 hours in dogs. Oral absorption in dogs, cats, and horses is approximately 100%.

## Indications and Clinical Uses

Tinidazole is indicated to treat diarrhea and other intestinal problems caused by intestinal protozoa such as *Giardia*, *Trichomonas*, and *Entamoeba*. Tinidazole also is active against many anaerobic bacteria and may be used as a substitute for metronidazole in small animals and horses for treatment of a variety of anaerobic infections.

### Precautionary Information

#### Adverse Reactions and Side Effects

Tinidazole has similar action as metronidazole. With high doses it can cause neurological problems, including ataxia, tremors, nystagmus, and seizures. The CNS signs are related to inhibition of action of gamma aminobutyric acid (GABA) and are responsive to benzodiazepines (diazepam). Like other nitroimidazoles, it has the potential to produce mutagenic changes in cells, but this has not been demonstrated in vivo. Like other nitroimidazoles, it has a bitter taste and can cause vomiting and anorexia. However, the bitter taste is not as bad as that of metronidazole.

#### Contraindications and Precautions

Do not administer to animals that may be prone to seizures. Do not administer to animals already known to be sensitive to metronidazole. Do not administer to pregnant animals.

#### Drug Interactions

Like other nitroimidazoles, it can potentiate the effects of warfarin and cyclosporine via inhibition of drug metabolism.

## Instructions for Use

Give oral dose with food to minimize the unpleasant taste and decrease nausea.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. Most anaerobic bacteria have MIC values below 2 mcg/mL.

## Formulations

- Tinidazole is available in 250- and 500-mg tablets.

## Stability and Storage

Tablets have been crushed and mixed with flavorings to improve palatability. These suspensions are stable for 7 days.

## Small Animal Dosage

### Dogs

- 15 mg/kg q12h PO.

### Cats

- 15 mg/kg q24h PO. Duration of therapy will depend on whether one is treating *Giardia* (5 days) or other anaerobic infections (longer than 5 days).

## Large Animal Dosage

### Horses

- 10-15 mg/kg q12h PO.

## Regulatory Information

Do not administer to animals that produce food. Administration of nitroimidazoles to animals intended for food is prohibited.

## Tobramycin Sulfate

toe-brah-mye'sin sul'fate

**Trade and other names:** Nebcin, Tobi (human nebulization product)

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Aminoglycoside antibacterial drug. Like other aminoglycosides, tobramycin is bactericidal. It binds to the 30S ribosomal subunit in bacteria to inhibit protein synthesis and lead to cell death. It is concentration dependent in its antibacterial action. Tobramycin has similar activity (MIC in same range) as gentamicin against *Klebsiella pneumoniae*, and *Escherichia coli*. Tobramycin is usually more active against *Pseudomonas aeruginosa* than gentamicin. Generally, if an organism is susceptible to tobramycin it will also be susceptible to amikacin. Tobramycin pharmacokinetics in animals indicates that it has similar clearance and distribution as other aminoglycosides. In horses the half-life was 4.6 hours, with a volume of distribution of 0.18 L/kg.

### Indications and Clinical Uses

Tobramycin, like other aminoglycosides, is used to treat serious systemic infections caused by gram-negative bacteria. It is often administered simultaneously with beta-lactam antibiotics to produce a synergistic effect. The infections treated include pneumonia, soft tissue infections, and sepsis. Like many off-label antibiotics in animals, the use in animals has been primarily derived from empirical use and from pharmacokinetic–pharmacodynamic information. Tobramycin has also been used topically. It has been used in nebulizing solutions for respiratory infections. For nebulization, there is a unique formulation used in people (Tobi) that is without preservatives and is intended to treat infections caused by *Pseudomonas aeruginosa* in the airways of cystic fibrosis patients. Following administration by this route, tobramycin remains concentrated primarily in the airways, and concentrations in plasma or serum are very low and unlikely to cause toxicity.

### Precautionary Information

#### Adverse Reactions and Side Effects

Nephrotoxicity is the most dose-limiting toxicity. Ensure that patients have adequate fluid and electrolyte balance during therapy. Ototoxicity and vestibulotoxicity also are possible.

#### Contraindications and Precautions

When used with anesthetic agents, neuromuscular blockade is possible. Do not mix in a vial or syringe with other antibiotics.

#### Drug Interactions

Avoid mixing in vials with other drugs. It is incompatible with other antibiotics and inactivation occurs rapidly.

### Instructions for Use

Inject intravenously or intramuscularly. Synergistic effects with beta-lactam antibiotics have been demonstrated in vitro, but it is not known if this translates to a clinical effect. For nebulization treatment of respiratory infections, dosing guidelines for animals have not been determined. In people (including pediatric patients), it is instructed to administer 300 mg of tobramycin (total dose) twice daily for 28 days. The solution used for nebulization (in individual packets with no preservatives) is called Tobi, but it is more expensive than injectable formulations. Tobramycin

injectable has been used instead, but it contains preservatives that could induce bronchospasm. Use diluted tobramycin with 3 mL of saline and administer albuterol before nebulization to decrease bronchospasm.

### **Patient Monitoring and Laboratory Tests**

Susceptibility testing: The CLSI MIC value break point for susceptibility is  $\leq 4$  mcg/mL. Monitor BUN, creatinine, and urine for evidence of renal toxicity. Blood concentrations can be monitored to detect problems with systemic clearance. When monitoring trough levels in a patient dosed once daily, the trough levels should be below the limit of detection. Alternatively, measure half-life from samples taken at 1 hour and 2-4 hours after dosing. Clearance should be above 1.0 mL/kg/min, and half-life should be less than 2 hours.

### **Formulations**

- Tobramycin is available in 40-mg/mL injections. The solution for nebulization (Tobi) is 60 mg per mL contained in 5-mL ampules.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Store powder at room temperature. Reconstituted solutions are stable for 24 hours at room temperature and 96 hours refrigerated. Do not use discolored solutions. Tobramycin sulfate diluted in fluids can be frozen and stable for 30 days. Ophthalmic solutions have been compounded and shown to be stable for 90 days. Do not mix in a vial or syringe with other antibiotics, especially beta-lactam agents (penicillins and cephalosporins) because inactivation may occur.

### **Small Animal Dosage**

#### **Dogs**

- 9-14 mg/kg q24h SQ, IM, or IV.
- Nebulization therapy is sometimes used in small animals. (See “[Instructions for Use](#)” section for details on nebulization therapy.)

#### **Cats**

- 5-8 mg/kg q24h SQ, IM, or IV.

### **Large Animal Dosage**

#### **Horses**

- 4 mg/kg will attain targeted concentrations for most bacteria, but to reach the target for bacteria at the breakpoint of 4 mcg/mL, a dose of 7.2 mg/kg is needed. These doses may be administered IV or IM once daily.

### **Regulatory Information**

Do not administer to animals intended for food or animals that produce food. Other drugs in this class require extralabel withdrawal times of 18 months.

## **Tocainide Hydrochloride**

toe-kay'nide hye-droe-klor'ide

**Trade and other names:** Tonocard

**Functional classification:** Antiarrhythmic

## Pharmacology and Mechanism of Action

Antiarrhythmic drug. Tocainide is a Class Ib antiarrhythmic. Like other Class I drugs, such as lidocaine, it blocks sodium channels in cardiac tissues and inhibits Phase 0 depolarization to suppress spontaneous depolarization.

## Indications and Clinical Uses

Tocainide is an oral substitute used for treatment and control of ventricular arrhythmias. The use in veterinary medicine has been uncommon. Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

### Precautionary Information

#### Adverse Reactions and Side Effects

In dogs, anorexia and GI toxicity have been reported. Arrhythmias, vomiting, and ataxia also are possible. (In one study, 35% of dogs showed GI effects.)

#### Contraindications and Precautions

Use cautiously in animals that are also receiving beta blockers. Do not use in patients with heart block.

#### Drug Interactions

No drug interactions have been reported for animals.

## Instructions for Use

Tocainide has limited experience in animals. However, clinical studies demonstrate efficacy.

## Patient Monitoring and Laboratory Tests

Therapeutic concentrations are 6-10 mcg/mL.

## Formulations

- Tocainide is available in 400- and 600-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 15-20 mg/kg q8h PO.

### Cats

- No dose has been established.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Toceranib Phosphate

toe-cer-a-nib

**Trade and other names:** Palladia

**Functional classification:** Anticancer agent



## Pharmacology and Mechanism of Action

Anticancer agent. For treatment of Grade II or III cutaneous mast cell tumors in dogs. Toceranib (Palladia) is a receptor tyrosine kinase (RTK) inhibitor that kills tumor cells and decreases the blood supply to the tumor. The antiangiogenic properties occur via inhibition of RTK activity (otherwise known as *vascular endothelial growth factor* [VEGF]). The effect of toceranib is to produce antiangiogenic and antiproliferative properties that limit growth of the tumor. Toceranib also produces a significant decrease in regulatory T-cells (Treg) in dogs with cancer, which may increase immune surveillance.

After administering toceranib to dogs, it is widely distributed (VD >20 L/kg) and has a half-life of approximately 16-17 hours. It has good oral absorption (77%) and high protein binding (91%-93%). Feeding does not affect oral absorption. High concentrations appear in the bile, liver, and feces and indicate that it is primarily eliminated by metabolism and there is little drug excreted in the urine (renal clearance is approximately 7%). Another drug that has been used for the same indication in dogs, but has a somewhat different mechanism of action is masitinib (Kinavet-CA1, Masivet). (See Masitinib section in this book for more details.)

## Indications and Clinical Uses

Toceranib is an approved anticancer agent for dogs. The use has been established in clinical studies for Grade II or III cutaneous mast cell tumors. Many dogs are also treated with corticosteroids (prednisolone). Although it is approved for mast cell tumors in dogs, some clinicians have used it to treat adenocarcinoma, melanoma, mammary carcinoma, soft tissue sarcoma, and anal gland adenocarcinoma; however, efficacy for these indications has not yet been established. There are no reports available to document efficacy or safety in cats.

### Precautionary Information

#### Adverse Reactions and Side Effects

Dogs with mast cell tumors often have GI problems associated with the tumor and treatment. Therefore many dogs are treated simultaneously with antihistamines and drugs to suppress stomach acid (e.g., H<sub>2</sub> blockers or proton pump inhibitors). The most common adverse effects are diarrhea, loss of appetite, lameness, weight loss, and blood in the feces. It should not be administered during pregnancy.

#### Contraindications and Precautions

Daily dosing should not be administered because of frequency of adverse events. People handling the drug, especially pregnant women, should receive proper instructions about the drug's adverse effects.

#### Drug Interactions

No drug interactions have been reported for animals. Metabolism is primarily via flavin monooxygenase (FMO), which is not typically involved in drug-drug interactions. It is not known if toceranib may be responsible for drug-drug interactions that involve the cytochrome P450 system.

## Instructions for Use

Toceranib is approved for cutaneous mast cell tumor in dogs. There is clinical use for other tumors, but efficacy has not yet been established for other uses. If adverse effects occur at the initial dose, a lower dose (e.g., 2.5 mg/kg) may be considered.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary. If assays are available, the targeted plasma drug concentration is 40 ng/mL or greater for 48 hours.

## Formulations

Toceranib is available in 10-, 15-, and 50-mg tablets, which are film coated and should not be split.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Toceranib is only soluble at low pH values (pH less than 3). If mixed in solutions, it will precipitate at higher pH values.

## Small Animal Dosage

### Dogs

- 3.25 mg/kg PO every other day. Medical oncologists may recommend a lower dosage of 2.5-3 mg/kg per dose and treat on a schedule of 3 days per week (Monday, Wednesday, Friday, for example). The minimum effective dose is 2.2 mg/kg every other day. If adverse reactions occur, discontinue the drug (for up to 2 weeks) and reinstate treatment at a lower dose.

### Cats

- No dose established.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Do not administer to food-producing animals.

## Toltrazuril

tole-traz'yoo'ril

**Trade and other names:** Baycox

**Functional classification:** Antiprotozoal

## Pharmacology and Mechanism of Action

Antiprotozoal drug. Coccidiostat. Toltrazuril is a triazinone effective for *Isospora* and coccidiosis, *Toxoplasma gondii*, and *Eimeria* spp. Toltrazuril is a derivative of another drug, ponazuril, that is also used for the same conditions. Toltrazuril sulfone (ponazuril) is found in serum and cerebrospinal fluid (CSF) of treated horses. See ponazuril section in this book for more details.

## Indications and Clinical Uses

Toltrazuril has been used as a treatment of equine protozoal myeloencephalitis (EPM) caused by *Sarcocystis neurona*. However, it is recommended to use an approved drug, ponazuril (Marquis), for treatment of horses. There has been limited experience in cats for treating toxoplasmosis.

## Precautionary Information

### Adverse Reactions and Side Effects

Administration of 50 mg/kg to horses (5 and 10 times the recommended dose) produced minor adverse effects, according to the manufacturer. There were minimal changes in the serum analysis.

**Contraindications and Precautions**

No contraindications are reported for animals.

**Drug Interactions**

No drug interactions have been reported in animals.

**Instructions for Use**

Although toltrazuril has been used in horses, the approved drug ponazuril is preferred for use.

**Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary.

**Formulations**

- Toltrazuril is not currently available in commercial formulations in the US for horses. It is available in suspension for poultry and livestock in other countries and has been imported to the US after permission from the FDA.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Cats**

- Treatment of toxoplasmosis: 5-10 mg/kg q24h PO for 2 days.

**Large Animal Dosage****Horses**

- EPM caused by *S. neurona*: 5-10 mg/kg (7.5 mg/kg for most horses) q24h PO for a minimum of 30 days.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Tramadol Hydrochloride**

tram'ah-dole

**Trade and other names:** Ultram, and generic brands; outside the US, Tramadon and Altadol

**Functional classification:** Analgesic

**Pharmacology and Mechanism of Action**

Analgesic. Tramadol is a racemic mixture (R & S) that has a complicated mechanism of action. It has some mu-opioid receptor action, but this effect is 10 times lower than codeine and 6000 times lower than morphine. Tramadol also inhibits the reuptake of norepinephrine (NE) and serotonin (5 HT) and produces secondary effects on alpha<sub>2</sub>-adrenergic receptors in pain pathways. One isomer has greater effect on 5 HT reuptake and greater affinity for mu-opiate receptors. The other isomer is more potent for NE reuptake and less active for inhibiting 5 HT reuptake. Taken together, the effects of tramadol may be explained through inhibition of 5 HT reuptake, action on alpha<sub>2</sub>-receptors, and mild activity on opiate mu-receptors, but the contribution of each of these mechanisms for treatment

of pain in animals is undetermined. Tramadol has as many as 11 metabolites. One metabolite (O-desmethyl tramadol, also called *M1*) may have greater opiate effects than the parent drug (for example, 200-300 times greater opiate effect than tramadol) but still lower than morphine. In animals that produce this metabolite in sufficient amounts, some analgesic action may be attributed to opiate-mediated effects from the active metabolite. The other metabolites have not been shown to have active analgesic activity.

The pharmacokinetics of tramadol and metabolites have been studied extensively in dogs, horses, and cats. The pharmacokinetics are inconsistent among studies, with variation in clearance, oral absorption, and metabolism to the active metabolite among studies within and between species. Most studies agree that the active metabolite (*M1*) in dogs is a minor metabolite and contributes little, if any, to the analgesic effects. In most studies the concentrations of this metabolite were either too low to quantify or nonexistent and may not contribute to the analgesic effects. Tramadol half-life in dogs is approximately 1.0-2.7 hours with oral absorption as high as 65%, but variable. In cats, the half-life is 3-4 hours and they produce higher and more sustained concentrations of the active metabolite (*M1*) than other animals—presumably because of differences in their ability to clear the metabolite. Active metabolite concentration in cats parallels the concentrations of tramadol. Horses produce only low or undetectable levels of the active metabolite. In horses, the oral absorption has been extremely variable, ranging from 3% to 64%, but in most studies it has been low. The half-life also has been highly variable in horses ranging from 2 to 10 hours in 9 studies. In most studies the half-life in horses is short: 2-2.5 hours.

A drug with similar structure and activity as tramadol is tapentadol (Nucynta). Tapentadol is used for moderate pain in people (50-200 mg q4-6h), but its use has not been reported in animals.

### Indications and Clinical Uses

Tramadol has been used as an analgesic in people, dogs, cats, horses, and minor species (e.g., rabbits, goats). It is an alternative to pure opiate analgesics and NSAIDs in patients that require treatment for mild-to-moderate pain. In people it is regarded as a mild analgesic, but the pharmacokinetics of tramadol are different in people compared with animals. Clinical effects in humans cannot necessarily be extrapolated to animals. In animal studies—both clinical and experimental—the results have been variable and inconsistent to demonstrate its effectiveness as an analgesic. The studies have varied in the dose, route, and pain stimulus evaluated. There has been some evidence of analgesia after administration for treating pain associated with elective surgery, but there is a lack of evidence for an antinociceptive effect when experimental models of pain have been used. When tested for treating osteoarthritis in dogs, efficacy has been poor or produced only mild benefit. When tested in dogs for treating pain from orthopedic surgery, the results have been inconsistent with some studies showing little benefit and other studies showing a mild benefit. The clearance is increased with repeated administration in dogs, which makes chronic treatment less effective than short-term treatment. Some studies that have demonstrated efficacy have used injectable formulations (at 2-4 mg/kg) rather than oral forms, but injectable formulations are not available in North America. It may be more effective when used with an NSAID or other analgesics such as ketamine or  $\alpha_2$ -agonists. Tramadol has also been administered by the epidural route (diluted in saline) in horses, dogs, and cats (1-2 mg/kg). Although some analgesic was documented in these studies, the effects and pharmacokinetics were similar to other parenteral routes of administration, and it is assumed that tramadol is rapidly distributed systemically after epidural administration.

Cats produce more of the active opiate metabolite (O-desmethyl tramadol) than other animal species. Tramadol administration may produce opiate effects in cats, and limited clinical trials suggest some efficacy. In horses the efficacy has been variable. It

may produce transient analgesia, but there has been significant variation among horses. When tested for treatment of laminitis in horses, it had only limited efficacy when used alone at a dose of 5 mg/kg.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

In cats, some vomiting, behavior changes, excitement, and mydriasis may be observed, which is dose related. Both euphoria and dysphoria have been observed in cats. In horses, there may be short-term (approximately 20-40 minutes) agitation, head nodding, decreased gut sounds, trembling, muscle fasciculations, tachycardia, sweating, and ataxia. The effects in horses are most prominent after a rapid IV injection and minimized if the injection is administered slowly over 10 minutes. In dogs, adverse effects have been rare. Some sedation has been observed, which is dose related. There have been minimal cardiovascular or GI problems in dogs. At very high doses in dogs, seizures may occur. If adverse effects occur, they are only partially antagonized by naloxone.

#### **Contraindications and Precautions**

Use cautiously with other drugs that have CNS-depressing effects, such as opiates,  $\alpha_2$ -agonists, or serotonin uptake inhibitors (e.g., antidepressants and behavior-modifying drugs). Tramadol may potentiate their actions. Metabolites may be eliminated via the urine. Use with caution in animals with kidney disease or seizure disorders.

#### **Drug Interactions**

No drug interactions have been reported in animals. However, because of multiple effects from tramadol (serotonin reuptake inhibition, adrenergic effects, and opiate effects), interactions are possible with other drugs that act via similar mechanisms. Serotonin syndrome is theoretically possible when used with other serotonin reuptake inhibitors, but such interactions have not been reported in animals. It has been used safely with NSAIDs. It has been administered with inhalant anesthetics without any signs of adverse drug interaction.

### **Instructions for Use**

Dosing information is based on experimental studies in dogs, cats, and horses and some clinical studies. In most animals the oral immediate-release tablets are administered either whole or crushed and mixed with a vehicle. In some countries an injectable formulation is available that has been injected IV, IM, SQ, and epidurally. Tramadol extended-release (ER) tablets have been used in people, but in dogs these tablets show delayed absorption and plasma levels five times less than people at equivalent (mg/kg) doses. Therefore ER tablets for people may be inequitable in dogs and cats.

### **Patient Monitoring and Laboratory Tests**

No specific monitoring is necessary. Tramadol is not routinely measured, but effective concentrations have been reported to be in the range of 200-400 ng/mL for tramadol and 20-40 ng/mL for the active metabolite (M1).

### **Formulations**

- Tramadol immediate-release tablets are available in 50-mg tablets. Tramadol ER is available in 100-, 200-, or 300-mg tablets. In the US, injectable formulations are not available. However, in Europe and other countries, an injectable formulation is available as a 50-mg/mL injection that can be diluted further in 0.9% saline solution for IV administration. Compounded formulations of tramadol have been prepared in sterile water at a concentration of 10 mg/mL. This solution is stable up to 1 year if stored in the refrigerator protected from light.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Tramadol is water soluble. When mixed with aqueous vehicles, it has maintained potency and been stable for weeks. However, stability of compounded formulations that may contain flavorings and other excipients has not been evaluated.

## Small Animal Dosage

### Dogs

- 5 mg/kg q6h-8h PO. If an injectable form is available, 4 mg/kg IV q6-8h.

### Cats

- Start at 2 mg/kg and increase up to 4 mg/kg q8-12h PO. When injectable forms have been available, it also has been injected at a dose of 2 mg/kg IV and 2-4 mg/kg SQ q8h.

## Large Animal Dosage

### Horses

- 2 mg/kg IV (slowly) and 4-5 mg/kg PO. In horses the optimum dosing interval is not known, but because of the short half-life, every 6 hours may be appropriate, and extended withdrawal times may not be necessary in food-producing animals. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Regulatory Information

Tramadol was moved to Drug Enforcement Administration (DEA)-controlled drug status in 2015. It is now a Schedule IV controlled drug.

It is not recommended for food animals, but the half-life in most animals is short, and extended withdrawal times may not be necessary in food-producing animals. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

## Trandolapril

tran-doe'lah-pril

**Trade and other names:** Mavik

**Functional classification:** Vasodilator, ACE inhibitor

## Pharmacology and Mechanism of Action

Like other ACE inhibitors, it inhibits conversion of angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor and will stimulate sympathetic stimulation, renal hypertension, and synthesis of aldosterone. The ability of aldosterone to cause sodium and water retention contributes to congestion. Trandolapril, like other ACE inhibitors, will cause vasodilation and decrease aldosterone-induced congestion, but ACE inhibitors also contribute to vasodilation by increasing concentrations of some vasodilating kinins and prostaglandins. Trandolapril is converted to active trandolaprilat after administration.

## Indications and Clinical Uses

Trandolapril, like other ACE inhibitors, is used for treatment of hypertension and for management of congestive heart failure (CHF). Compared to other ACE inhibitors, such as enalapril or benazepril, it is not used commonly in veterinary medicine, and the use has been derived from anecdotal experiences.

**Precautionary Information****Adverse Reactions and Side Effects**

Trandolapril may cause azotemia in some patients; carefully monitor patients receiving high doses of diuretics. When administered with diuretics (furosemide) the renin-angiotensin-aldosterone system (RAAS) may be activated.

**Contraindications and Precautions**

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs may decrease vasodilating effects. Discontinue ACE inhibitors in pregnant animals; they cross the placenta and have caused fetal malformations and death of the fetus.

**Drug Interactions**

Use cautiously with other hypotensive drugs and diuretics. Nonsteroidal anti-inflammatory drugs may decrease vasodilating effects.

**Instructions for Use**

It has not been used extensively in veterinary patients. Most of the experience has been extrapolated from uses in people.

**Patient Monitoring and Laboratory Tests**

Monitor patients carefully to avoid hypotension. With all ACE inhibitors, monitor electrolytes and renal function 3-7 days after initiating therapy and periodically thereafter.

**Formulations Available**

- Trandolapril is available in 1-, 2-, and 4-mg tablets.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage**

- The dose has not been established for dogs. The dose in people is 1 mg/person/day to start, then increased to 2-4 mg/day.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

**Trazodone Hydrochloride**

Traz'-oh-done

**Trade and other names:** Desyrel and generic

**Functional classification:** Antianxiety agent, behavioral modification

**Pharmacology and Mechanism of Action**

Trazodone is an antianxiety agent. It is a triazolopyridine derivative and belongs to the phenylpiperazine group of centrally acting drugs. It acts both as a serotonin 2A

(5-HT<sub>2A</sub>) receptor antagonist and a (weak) selective serotonin reuptake inhibitor (SSRI), with little effect on dopamine. It also has nonspecific sedating properties and is used as a sedative and hypnotic. It has an active metabolite that also may have effects on the serotonin-1 receptor. The action as an antidepressant and anxiolytic agent appears to be distinct from tricyclic antidepressants and SSRIs. It is highly metabolized in people, but the metabolism and pharmacokinetics are not well understood in animals. The half-life is 6-9 hours in people. In dogs the half-life is 2.8 hours, with 85% oral absorption. When administered with food to dogs, it has a peak at 7 hours, with high variation. There have been preliminary studies in cats in which it appears to be well absorbed orally and has a sufficiently long half-life for treatment of anxiety and behavior problems.

### Indications and Clinical Uses

Trazodone has been used in dogs for events that trigger anxiety such as visits to the veterinarian, separation anxiety, thunderstorms, noise phobias, travel in a car, and other phobias and generalized anxiety events. Although trazodone has been helpful to relieve anxiety in these situations, it has a delayed onset of activity and can be unpredictable. To optimize the effects, it should be administered approximately 1 hour prior to an anticipated anxiety-inducing event. It also has been used to calm anxious dogs to restrict activity after surgery in order to facilitate confinement tolerance.

In cats it has been used for temporary sedation and to facilitate events that may produce anxiety, such as to facilitate transportation of cats.

### Precautionary Information

#### Adverse Reactions and Side Effects

Although use has been limited, trazodone has been used in dogs without reports of serious adverse effects. The most common effect is sedation at higher doses, which is not always an undesirable event. It has been used in some dogs safely for 28 days at doses of 7-10 mg/kg q8-12h. It may have fewer anticholinergic effects than tricyclic antidepressants. It has not produced adverse cardiac effects or seizure activity. When administered intravenously to dogs, adverse effects are more likely, which include aggression, behavior changes, and tachycardia.

In cats, clinical studies with a dose of 100 mg per cat did not produce any adverse effects such as anorexia, vomiting, diarrhea, ataxia, tremor, paradoxical excitation, or behavioral disinhibition. No laboratory test abnormalities or physical exam changes were observed in any cat.

#### Contraindications and Precautions

Because of the effect of trazodone on serotonin metabolism, reuptake, and receptors, its use with other drugs that affect serotonin should be done with caution. Serotonin syndrome effects have not been observed in dogs, but it should be used cautiously with drugs such as SSRIs (fluoxetine, paroxetine), tricyclic antidepressants (clomipramine), tramadol, and monoamine oxidase inhibitors (selegiline). Do not administer intravenously to dogs.

#### Drug Interactions

Trazodone is highly metabolized by cytochrome P450 enzymes. Such enzymes can be inhibited or induced by coadministration with other drugs. Although specific drug interactions have not been reported for dogs, there should be caution when administering to animals receiving other drugs known to affect cytochrome P450 enzymes.



## Instructions for Use

Start with a low dose in dogs (approximately 5 mg/kg) and work up gradually to higher doses as needed. In dogs, the starting dose is generally 25 or 50 mg per dog (depending on dog's size) once or twice per day and increase gradually. Compared to other behavior-modifying drugs such as SSRIs and tricyclic antidepressants, trazodone has a more rapid onset of effect. It may be administered 1 hour prior to an anticipated event that elicits anxiety in an animal such as thunderstorms, loud noises, car ride, or visit to the veterinarian. It may be administered with benzodiazepine drugs.

In cats it may be administered up to doses of 100 mg per cat. When administered to cats, it may be mixed with food to facilitate dosing. After dosing to cats, it will produce significant sedation and decreased activity. Peak sedation occurs between 2 and 2.5 hours.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- It is available as 50-, 100-, 150-, and 300-mg tablets.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 5 mg/kg PO as needed, but generally every 8-24 hours; or administer a single dose 1 hour prior to an anticipated event that may trigger anxiety. A typical dose for dogs is 7 mg/kg q12h. Alternatively, to avoid breaking tablets, give 25 or 50 mg per dog (depending on dog's size) once daily and increase gradually to a maximum of 600 mg per dog per day.

### Cats

- 50-100 mg per cat PO (peak effect occurs in 2-2.5 hours).

## Large Animal Dosage

- No dose is established for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Triamcinolone Acetonide, Triamcinolone Hexacetonide, Triamcinolone Diacetate

trye-am-sin'oh-lone

**Trade and other names:** Vetalog, TriamTabs, Aristocort, and generic brands

**Functional classification:** Corticosteroid

## Pharmacology and Mechanism of Action

Glucocorticoid anti-inflammatory drug. Anti-inflammatory effects are complex, but they are primarily via inhibition of inflammatory cells and suppression of expression of inflammatory mediators. There is disagreement on the potency of triamcinolone. Most human references indicate that triamcinolone has potency that is approximately

equal to methylprednisolone (about 5 times cortisol and 1.25 times prednisolone). However, many veterinary dermatologists suggest that potency is higher—6 to 10 times more potent—than prednisolone or approximately equal to dexamethasone. Thus the feline dose listed reflects this higher potency. Triamcinolone acetonide is often used for local treatment or to produce a sustained concentration. It is an injectable suspension that is slowly absorbed from the IM or intralesional injection site.

## Indications and Clinical Uses

Triamcinolone, like other corticosteroids, is used to treat inflammatory and immune-mediated diseases in animals. It is used for similar purposes as prednisolone and is an acceptable substitute for prednisolone in cats. The long-acting injectable formulation (triamcinolone acetonide) is used for intralesional therapy of tumors and similar purposes as methylprednisolone acetate. Large animal uses include treatment of inflammatory conditions and of recurrent airway disease (RAO), formerly called *chronic obstructive pulmonary disease* (COPD), in horses. Triamcinolone acetonide is also given intraarticularly to horses for treatment of arthritis.

## Precautionary Information

### Adverse Reactions and Side Effects

Side effects from corticosteroids are many and include polyphagia, polydipsia/polyuria, and hypothalamic–pituitary adrenal (HPA) axis suppression. Adverse effects include GI ulceration, hepatopathy, diabetes, hyperlipidemia, decreased thyroid hormone, decreased protein synthesis, impaired wound healing, and immunosuppression. When triamcinolone acetonide is used for ocular injections, there is some concern that granulomas may occur at the injection site. In horses, adverse effects include increased risk of laminitis, although evidence for this effect has been controversial.

### Contraindications and Precautions

Use cautiously in patients prone to ulcers or infection, or in animals in which wound healing is necessary. Use cautiously in animals with diabetes or renal failure, or in pregnant animals.

### Drug Interactions

Use cautiously, if at all, with NSAIDs because it may potentiate the GI toxicity.

## Instructions for Use

Triamcinolone, like other corticosteroids such as prednisolone, is administered in a variety of doses, depending on the severity of the condition being treated. Note that cats may require higher doses than dogs (sometimes twice as high).

## Patient Monitoring and Laboratory Tests

Monitor liver enzymes, blood glucose, and renal function during therapy. Monitor patients for signs of secondary infections. Perform an adrenocorticotropic hormone (ACTH) stimulation test to monitor adrenal function.

## Formulations

- Vetalog (veterinary preparation) is available in 0.5- and 1.5-mg tablets. Human preparation of triamcinolone has been available in 1-, 2-, 4-, 8-, and 16-mg tablets, but many tablet sizes have been discontinued.
- Triamcinolone hexacetonide is available in a 20-mg/mL suspension.
- Triamcinolone diacetate is available in a 25-mg/mL suspension.
- Triamcinolone acetonide is available in 10- or 40 mg/mL suspension (human form), or 2 and 6 mg/mL suspension (veterinary form).

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

- Dogs: For anti-inflammatory treatment, start with 0.1-0.2 mg/kg per day PO, then gradually taper to 0.1 mg/kg every other day. Eventually, some conditions can be controlled with 0.03-0.055 mg/kg q48h PO. (The manufacturer recommends doses of 0.11-0.22 mg/kg/day.)
- Cats: For anti-inflammatory treatment, start with 0.2 mg/kg per day PO. Gradually taper to a dose of 0.1 mg/kg (0.5 mg per cat—one tablet—is a common dose) every other day. Some cats can be controlled with low doses of 0.05 mg/kg q48h.
- Immune-mediated disease (dogs and cats): triamcinolone tablets at doses of 0.2-0.6 mg/kg/day, with maintenance doses of 0.1-0.2 mg/kg q48h PO.
- Triamcinolone acetonide: 0.1-0.2 mg/kg IM or SQ; repeat in 7-10 days.
- Intralesional: 1.2-1.8 mg or 1 mg for every centimeter diameter of tumor q2wks.

## Large Animal Dosage

### Horses

- 0.5-1 mg/kg q12-24h PO.
- Triamcinolone acetonide suspension: 0.022-0.044 mg/kg as a single dose IM.
- RAO: 0.09 mg/kg IM as a single dose.
- Intraarticular: 6-18 mg as a total dose (usually 9-12 mg). Repeat in 4-13 days if necessary.

### Cattle

- Induction of parturition: 0.016 mg/kg IM 1 week before induction of parturition with dexamethasone.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Triamterene

trye-am'ter-een

**Trade and other names:** Dyrenium

**Functional classification:** Diuretic

## Pharmacology and Mechanism of Action

Potassium-sparing diuretic. Triamterene has similar action to spironolactone, except that spironolactone has a competitive inhibiting effect on aldosterone; triamterene does not.

## Indications and Clinical Uses

Triamterene has been used infrequently in veterinary medicine. For treating congestive diseases, spironolactone is used more frequently. Use of triamterene in animals is derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness.

## Precautionary Information

### Adverse Reactions and Side Effects

Triamterene can produce hyperkalemia in some patients.

### Contraindications and Precautions

Do not use in dehydrated patients. Nonsteroidal anti-inflammatory drugs may interfere with action. Avoid supplements that are high in potassium.

### Drug Interactions

No specific drug interactions are reported for animals. However, use cautiously with other drugs that may contain potassium or cause potassium retention. Such drugs include trimethoprim.

## Instructions for Use

There is little clinical experience available for triamterene. There is no convincing evidence that triamterene is more effective than spironolactone.

## Patient Monitoring and Laboratory Tests

Monitor hydration status, serum potassium levels, and renal function.

## Formulations

- Triamterene is available in 50- and 100-mg capsules.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs and Cats

- 1-2 mg/kg q12h PO.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Trientine Hydrochloride

trye-en'teen hye-droe-klor'ide

**Trade and other names:** Syprine

**Functional classification:** Antidote

## Pharmacology and Mechanism of Action

Chelating agent. Trientine chelates copper to enhance its clearance in the urine. It may be more potent than penicillamine.

## 810 Trifluoperazine Hydrochloride

### Indications and Clinical Uses

Trientine is used to chelate copper when penicillamine cannot be tolerated in a patient. Use in animals has been primarily derived from empirical use and experience in humans. It may produce fewer GI problems compared with penicillamine.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals.

#### Contraindications and Precautions

Do not administer to pregnant animals; it may be teratogenic.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Trientine is used only in patients that cannot tolerate penicillamine.

### Patient Monitoring and Laboratory Tests

Monitor copper levels in treated patients.

### Formulations

- Trientine is available in 250-mg capsules.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 10-15 mg/kg q12h PO 1-2 hours before feeding.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Trifluoperazine Hydrochloride

trye-floo-oh-pare'ah-zeen hye-droe-klor'ide

**Trade and other names:** Stelazine

**Functional classification:** Antiemetic, phenothiazine

### Pharmacology and Mechanism of Action

Phenothiazine. Like other phenothiazines, it is a central-acting dopamine ( $D_2$ ) antagonist and suppresses dopamine activity in the CNS to produce sedation and prevent vomiting. Other phenothiazines include acepromazine, chlorpromazine, perphenazine, prochlorperazine, promazine, and propioperazine.

## Indications and Clinical Uses

Trifluoperazine is used for treatment of anxiety, to produce sedation, and as an anti-emetic. It is a weaker sedative than some of the other phenothiazines. In people it is used to treat psychotic disorders. Use in animals has been primarily derived from empirical use and experience in humans.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals but are expected to be similar to other phenothiazines. Phenothiazines can lower the seizure threshold in susceptible animals, although this is controversial for acepromazine. They can also cause sedation as a common side effect and extrapyramidal side effects (involuntary muscle movements) in some individuals.

#### Contraindications and Precautions

Use cautiously in patients that are hypotensive.

#### Drug Interactions

No drug interactions have been reported in animals. However, these drugs may be subject to cytochrome P450 drug interactions.

## Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Trifluoperazine is available in a 10-mg/mL oral solution; 1-, 2-, 5-, and 10-mg tablets; and 2-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Trifluoperazine is soluble in water and slightly soluble in ethanol. It is oxidized rapidly if exposed to air or light.

## Small Animal Dosage

### Dogs and Cats

- 0.03 mg/kg q12h IM.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

## Triflupromazine Hydrochloride

trye-floo-proe'mah-zeen hye-droe-klor'ide

**Trade and other names:** Vesprin and fluopromazine (former name)

**Functional classification:** Antiemetic, phenothiazine

### Pharmacology and Mechanism of Action

Phenothiazine. Central-acting dopamine ( $D_2$ ) antagonist. Triflupromazine suppresses dopamine activity in the CNS to produce sedation and prevent vomiting. Compared with other phenothiazines, triflupromazine may have stronger antimuscarinic activity. Other phenothiazines include acepromazine, chlorpromazine, perphenazine, prochlorperazine, promazine, and propiopromazine.

### Indications and Clinical Uses

Triflupromazine is used to produce sedation and as an antiemetic. In people it is used to treat psychotic disorders. Use in animals has been primarily derived from empirical use and experience in humans. Little information on animal use is available.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals but are expected to be similar to other phenothiazines. Phenothiazines can lower the seizure threshold in susceptible animals. They can also cause sedation as a common side effect and extrapyramidal side effects (involuntary muscle movements) in some individuals.

#### Contraindications and Precautions

Use cautiously in patients that are hypotensive.

#### Drug Interactions

No drug interactions have been reported in animals. However, these drugs may be subject to cytochrome P450 drug interactions.

### Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Triflupromazine is available in 10- and 20-mg/mL injections.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs and Cats

- 0.1-0.3 mg/kg q8-12h IM.

### Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 2

## Trilostane

trye'loe-stane

**Trade and other names:** Modrenal and Vetoryl

**Functional classification:** Adrenal suppressant

## Pharmacology and Mechanism of Action

Trilostane inhibits synthesis of cortisol in dogs. It is a competitive inhibitor of 3-beta-hydroxysteroid dehydrogenate, which will interfere with the steps that lead to cortisol secretion from the adrenal cortex. Inhibition of cortisol is dose dependent and reversible. Compared with mitotane, which destroys adrenocortical cells, trilostane produces a transient decrease in cortisol. The enzyme affected by trilostane is also involved with synthesis of aldosterone, corticosterone, and androstenedione. It also affects conversion of pregnenolone to progesterone. Ordinarily, the zona glomerulosa is spared from trilostane effects; but, aldosterone production may be affected in some dogs. Therefore other hormones also may be decreased from treatment with trilostane.

## Indications and Clinical Uses

Trilostane is used to treat hypercortisolemia (hyperadrenocorticism) in dogs (Cushing disease). Peak concentrations of trilostane occur at approximately 2 hours after an oral dose. Cortisol concentrations will decrease as early as 7-10 days after initiating treatment with trilostane. It is reported to improve polyuria, polydipsia, and polyphagia in 70%-80% of dogs with PDH. Treatment with mitotane has been compared with trilostane, and it has been shown that each drug, although acting through different mechanisms, produces similar survival times in dogs with PDH. Other drugs used to treat canine Cushing disease include mitotane (Lysodren), selegiline (Anipryl), and ketoconazole—all drugs acting through different mechanisms. Treatment of alopecia X in dogs (Pomeranians and poodles) has been effective in most animals (9-12 mg/kg/day PO).

Trilostane also has been effective in cats with no reported adverse effects. Trilostane can decrease clinical signs of hyperadrenocorticism in cats and can improve regulation of diabetes, which is often found concurrently in these cats.

In horses, it has been used to treat PPID (equine Cushing disease), and there is preliminary evidence of some benefit (improved clinical signs, reduced laminitis, reduced cortisol) from trilostane at a dose of 1 mg/kg per day PO.

## Precautionary Information

### Adverse Reactions and Side Effects

In some dogs, transient lethargy, anorexia, or vomiting is observed, which may be caused by excessive cortisol suppression. If excessive cortisol suppression has occurred, oral prednisolone/prednisone can be administered and the dog should improve within 2 hours. When the trilostane is again reintroduced, the dose should be reduced. Glucocorticoid or mineralocorticoid deficiency or development of adrenal gland necrosis has been associated with trilostane treatment.



Trilostane may decrease aldosterone in some dogs; therefore dehydration, weakness, hyponatremia, and hyperkalemia is possible and may be observed in some dogs sensitive to the mineralocorticoid inhibition.

Although the effects of trilostane are ordinarily transient and reversible, some dogs have had irreversible adrenal gland necrosis from trilostane. These dogs must be managed for hypoadrenocorticism.

### **Contraindications and Precautions**

Trilostane may decrease synthesis of adrenocortical hormones. Use cautiously in animals with low potassium concentrations. Do not administer to animals with kidney or liver disease, and do not administer to animals intended for breeding.

### **Drug Interactions**

Use cautiously, if at all, with aldosterone antagonists, such as spironolactone. If administered with ACE inhibitors, there is a risk of hyperkalemia.

## **Instructions for Use**

Adjust dose as needed by monitoring cortisol concentrations. Trilostane is a short-acting drug with a peak effect at approximately 4 hours and duration of 8-10 hours. Administer with food if possible. Most dogs can be controlled with once-daily treatment at a starting dose of 2-3 mg/kg once daily (manufacturer's range is 3-6 mg/kg once a day). However, in some dogs 24-hour cortisol suppression does not occur; therefore, consider administration twice daily in patients that are not adequately controlled in order to improve clinical control. When using twice-daily treatment, a starting dose of 0.5-1 mg/kg q12h PO can be used and gradually increased to 1.5-3 mg/kg q12h PO. In some dogs, administration three times daily may be needed. In cats, once-daily dosing can be considered, but many cats are better controlled with twice-daily administration. If the cat is also receiving insulin twice daily, the trilostane should also be given twice daily to coincide with the insulin treatment.

## **Patient Monitoring and Laboratory Tests**

Monitor cortisol concentrations in treated animals starting at approximately 10-14 days after starting treatment, then approximately every 3 months. Clinical signs such as the patient's thirst, urination habits, appetite, and skin condition also should be monitored during treatment. The baseline serum cortisol—collected preferably at 4-6 hours after trilostane administration—can be used to monitor effectiveness of trilostane therapy. The ideal target range is 1.3-2.9 mcg/dL (35-80 nmol/L), or  $\leq 50\%$  of the pretreatment baseline cortisol concentration.

If further evaluation is needed, use the ACTH stimulation test. Perform testing at peak trilostane concentrations of 4-6 hours after trilostane administration. (Alternatively, some endocrinologists recommend 2-4 hours after trilostane administration.) Cortisol concentrations of 1.45-5.4 mcg/dL (40-150 nmol/L) have been considered adequate after ACTH stimulation. If cortisol is too low, consider lowering the dose; if cortisol is too high, consider increasing the dose. Monitor sodium and potassium concentrations in treated dogs. If necessary, supplement with potassium because of aldosterone inhibition. Measurement of endogenous ACTH is not recommended for testing response to trilostane.

## **Formulations**

Veterinary formulations approved in the US and Europe include capsules of 10, 30, 60, and 120 mg.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

## Small Animal Dosage

### Dogs

- 3-6 mg/kg once per day PO. Many dogs are controlled with a lower dose of 1.5-3 mg/kg q12h PO.

Adjust dose based on cortisol measurements.

Large dogs (>30 kg) may require lower dose compared to small dogs (<15 kg). The following dose schedule is based on dog weight:

- Dogs 4.5-10 kg: 30 mg q24h PO.
- Dogs 10-20 kg: 60 mg q24h PO.
- Dogs 20-40 kg: 120 mg q24h PO.
- Dogs 40-60 kg: 180 mg q24h PO.
- Treatment of alopecia X: 9-12 mg/kg/day PO.

### Cats

- 3-6 mg/kg q24h PO and gradually increase (as needed) to 10 mg/kg q24h.
- Some cats are better controlled with twice-daily administration. In these cats, start with 3 mg/kg q12h PO, then reevaluate and increase dose to 5 mg/kg q12h PO as needed.

## Large Animal Dosage

### Horses

- 0.4-1 mg/kg/day PO (added to feed).

## Regulatory Information

Trilostane should not be used in animals that produce food.

## Trimeprazine Tartrate and Trimeprazine-Prednisolone

trye-mep'rah-zeen tar'trate

**Trade and other names:** Temaril, Panectyl (in Canada), alimemazine, and Temaril-P (with prednisolone)

**Functional classification:** Antiemetic, phenothiazine

## Pharmacology and Mechanism of Action

Phenothiazine with antihistamine activity. It has actions similar to other antihistamines, but it also produces sedation similar to other phenothiazines.

## Indications and Clinical Uses

Trimeprazine is used alone or in combination with corticosteroids for inflammatory and allergic problems. The most common use is for pruritus in dogs in combination with prednisolone (Temaril-P). It also has been used for treating motion sickness and is approved in combination with prednisolone as an antitussive in dogs. The combination Temaril-P with prednisolone also is approved to treat pruritus in animals. Therapeutic effect is attributed to the combined antihistamine and sedative effect of

## 816 Trimeprazine Tartrate and Trimeprazine-Prednisolone

trimeprazine and the anti-inflammatory effect of prednisolone. This combination may be more effective for pruritus than prednisolone alone.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are attributed to the antihistamine and phenothiazine effects. The most common is sedation, but ataxia and behavior changes also can occur.

#### Contraindications and Precautions

Phenothiazines can potentially lower seizure threshold in sensitive animals, although this has not been shown for acepromazine in animals and has not been reported for trimeprazine.

#### Drug Interactions

No drug interactions have been reported for animals.

### Instructions for Use

There is evidence that trimeprazine is more effective when combined with prednisolone for treatment of pruritus. The combination product is Temaril-P, which contains trimeprazine and prednisolone.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Trimeprazine is available in 2.5-mg/5-mL syrup and 2.5-mg tablets.
- Temaril-P is available in tablets that contain 5 mg trimeprazine + 2 mg prednisolone. Capsules are available with 3.75 mg trimeprazine + 1 mg prednisolone and 7.5 mg trimeprazine + 2 mg prednisolone.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 0.5 mg/kg q12h PO.
- Prednisolone + trimeprazine: Start with 0.5 mg/kg prednisolone + 1.25 mg/kg trimeprazine per day. Taper dose to 0.3 mg/kg prednisolone + 0.75 mg/kg trimeprazine once daily or once every other day PO.
- Tablet equivalents: One-half tablet for dogs <4.5 kg; one tablet for dogs 5-9 kg; two tablets for dogs 10-18 kg; and three tablets for dogs >20 kg. All doses started with twice daily and eventually tapered to once daily and once every other day.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

RCI Classification: 4

## Trimethobenzamide

trye-meth-oh-ben'zah-mide

**Trade and other names:** Tigan

**Functional classification:** Antiemetic

### Pharmacology and Mechanism of Action

Antiemetic. Trimethobenzamide inhibits vomiting at the chemoreceptor trigger zone (CRTZ).

### Indications and Clinical Uses

Trimethobenzamide is used for antiemetic treatment, especially when vomiting is induced from the CRTZ (e.g., from chemotherapeutic drugs). Use in animals has been primarily derived from empirical use and experience in humans. There are no well-controlled clinical studies or efficacy trials to document clinical effectiveness. Other antiemetics (e.g., maropitant) are more often used in dogs and cats.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects not reported in animals.

#### Contraindications and Precautions

Not recommended for use in cats.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

Efficacy as antiemetic not reported in animals.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

- Trimethobenzamide is available in 100-mg/mL injections and 100- and 250-mg capsules.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 3 mg/kg q8h IM or PO.

#### Cats

- Not recommended.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Trimethoprim Sulfadiazine

trye-meth'oh-prim + sul-fah-dye'ah-zeen

**Trade and other names:** Tribissen, Uniprim, Tucoprim, Equisul-SDT, and Di-Trim

**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Trimethoprim + sulfonamides combine the antibacterial drug action of trimethoprim and a sulfonamide. The activity is attributed to their synergistic effect in inhibiting folic acid metabolism in bacteria. Sulfonamides are competitive inhibitors of dihydrofolate synthesis. Trimethoprim inhibits the enzyme dihydrofolate reductase. When used in combination, it has a broad spectrum of activity against susceptible bacterial infections (gram-negative and gram-positive). Trimethoprim + sulfadiazine is only available as a veterinary preparation; trimethoprim + sulfamethoxazole is a human preparation. There are no published reports of differences in efficacy between trimethoprim + sulfadiazine versus trimethoprim + sulfamethoxazole. The primary difference between sulfamethoxazole and sulfadiazine is that sulfamethoxazole is metabolized more extensively and sulfadiazine may attain higher active urine concentrations in some patients. The pharmacokinetics vary among species and routes of administration. In most animals the trimethoprim is eliminated faster than the sulfonamide component. The combination is administered as a 1:5 ratio (trimethoprim:sulfonamide), but the ratio after administration varies considerably to 1:20 or lower. A ratio of 1:20 has been suggested as optimum for antibacterial effects, but this ratio has not been confirmed in clinical studies in animals.

In horses the average half-life of trimethoprim is 3 hours and sulfadiazine is 7.8 hours.

### Indications and Clinical Uses

Trimethoprim + sulfadiazine is used to treat a variety of infections in dogs, cats, horses, and some exotic animals. The combination has efficacy for susceptible bacterial infections (gram negative and gram positive), including respiratory infections, soft tissue and skin infections, wounds, abscesses, and urogenital infections. In horses, the combination has been used for respiratory infections, joint infections, abdominal infections, prostate infections, soft tissue infections, and infections of the CNS. In horses it is approved for treatment of respiratory infections caused by *Streptococcus equi* for 10 days. The combination also is used occasionally for infections caused by protozoa (e.g., coccidial and *Toxoplasma* infections). The combination has not been successful for treating infections in abscesses or infections caused by anaerobic bacteria, possibly because of interactions with material in necrotic tissues.

### Precautionary Information

#### Adverse Reactions and Side Effects

In horses, oral administration of trimethoprim + sulfonamides may be associated with diarrhea. Other effects observed in horses include idiosyncratic neurological reactions consisting of behavior changes, gait abnormalities, and hyperesthesia. These effects improved soon after discontinuing the medication. Adverse effects associated with sulfonamides in dogs include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites; therefore more toxic metabolite may accumulate in some animals.

Consult other sections of this handbook for additional descriptions of adverse reactions from sulfonamides for individual drugs. Trimethoprim + sulfonamides may decrease thyroid hormone after treatment in dogs. Effects on thyroid function are most apparent after 2 weeks of treatment, but they are reversible.

### Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed. If diarrhea develops in horses, discontinue treatment.

*Pregnancy precaution:* Use in pregnant mares is justified when the benefits outweigh the risk to the fetus. Use of potentiated sulfonamides during pregnancy has been associated with increased risk of congenital abnormalities that may be caused by folate deficiency. In humans, sulfonamides exposure to the newborn (via placenta and milk) can cause hyperbilirubinemia-induced neurotoxicity. However, this syndrome has not been described in animals.

### Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for IV forms of trimethoprim + sulfonamides.

## Instructions for Use

Dose listed is of the combined components; 30 mg/kg = 5 mg/kg trimethoprim and 25 mg sulfonamide. There is evidence that 30 mg/kg/day is efficacious for pyoderma; for other infections, 30 mg/kg twice daily has been recommended. Oral trimethoprim is not absorbed in ruminants.

## Patient Monitoring and Laboratory Tests

Culture and susceptibility testing: All susceptibility testing is based on a 1:19 ratio of trimethoprim:sulfonamide. CLSI break point for susceptible organisms is  $\leq 2/38$  mcg/mL. For streptococci, this break point is  $\leq 2/38$  mcg/mL. Values listed are the concentration of trimethoprim/sulfonamide ratio. Trimethoprim + sulfonamides may affect the monitoring of thyroid hormones. In dogs, trimethoprim + sulfadiazine may cause a functional hypothyroidism and lower total  $T_4$  concentrations. Trimethoprim + sulfamethoxazole decreased thyroid function at 30 mg/kg q12h and also at 15 mg/kg q12h. Trimethoprim + sulfadiazine at 15 mg/kg q12h for 4 weeks did not affect thyroid function in one study. Effects of trimethoprim + sulfonamides on thyroid function in dogs are reversible. In horses, trimethoprim + sulfadiazine did not affect assays of thyroid function.

## Formulations

- Trimethoprim + sulfadiazine is available in 30-, 120-, 240-, 480-, and 960-mg tablets. (All formulations have a ratio of 5:1, sulfadiazine to trimethoprim.) Recently, tablets have become less available. It is also available as an oral paste and suspension (333 mg sulfadiazine + 67 mg trimethoprim) for horses. As a powder for horses, each gram contains 67 mg trimethoprim and 333 mg of sulfadiazine. It has also been available as a 48% injectable suspension for horses, but availability of injectable formulations has diminished.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

**Small Animal Dosage****Dogs and Cats**

- Doses are listed as the combined sulfonamide + trimethoprim.
- 15 mg/kg q12h PO or 30 mg/kg q12-24h PO.
- *Toxoplasma*: 30 mg/kg q12h PO.

**Large Animal Dosage****Horses**

- The approved label dose for the oral suspension is 24 mg/kg (20 mg/kg sulfadiazine + 4 mg/kg trimethoprim) twice daily for 10 days. Generally, the dose ranges from 25-30 mg/kg (approximately 25 mg sulfonamide + 5 mg trimethoprim) q12h PO for most treatments.

**Cattle**

- No dose has been established. Trimethoprim is not absorbed orally in ruminants, but it is absorbed in calves. Trimethoprim + sulfadoxine has been used in cattle (16 mg/kg combined drug every 24 hours IV or IM), but this drug is not available in the US.

**Regulatory Information**

Withdrawal times are not available. Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle. Do not use in horses intended for food.

**Trimethoprim + Sulfamethoxazole**

trye-meth'oh-prim + sul-fah-meth-oks'ah-zole

**Trade and other names:** Bactrim, Septra, and generic brands

**Functional classification:** Antibacterial

**Pharmacology and Mechanism of Action**

Trimethoprim + sulfonamides combine the antibacterial drug action of trimethoprim and a sulfonamide. The activity is attributed to their synergistic effect in inhibiting folic acid metabolism in bacteria. Sulfonamides are competitive inhibitors of dihydrofolate synthesis. Trimethoprim inhibits the enzyme dihydrofolate reductase. When used in combination, it has a broad spectrum of activity against susceptible bacterial infections (gram negative and gram positive). Trimethoprim has been combined with both sulfadiazine and sulfamethoxazole. Trimethoprim + sulfadiazine is only available as a veterinary preparation; trimethoprim + sulfamethoxazole is a human preparation. There are no published reports of differences in efficacy between trimethoprim + sulfadiazine versus trimethoprim + sulfamethoxazole. The primary difference between sulfamethoxazole and sulfadiazine is that sulfamethoxazole is metabolized more extensively. Sulfadiazine may attain higher active urine concentrations in some patients. The combination is administered as a 1:5 ratio (trimethoprim to sulfonamide), but the ratio after administration varies considerably to 1:20 or lower. A ratio of 1:20 has been suggested as optimum for antibacterial effects, but this ratio has not been confirmed in clinical studies in animals.

## Indications and Clinical Uses

Trimethoprim + sulfamethoxazole is used to treat a variety of infections in dogs, cats, horses, and some exotic animals. Trimethoprim + sulfamethoxazole is used for treatment of UTIs, skin and soft tissue infections, prostate infections, pneumonia, and CNS infections. In horses, they have been used for respiratory infections, joint infections, abdominal infections, soft tissue infections, and infections of the CNS. The combination has not been successful for treating infections in abscesses or infections caused by anaerobic bacteria. The combination also is used occasionally for infections caused by protozoa (e.g., coccidial and *Toxoplasma* infections).

## Precautionary Information

### Adverse Reactions and Side Effects

In horses, oral administration of trimethoprim + sulfonamides may be associated with diarrhea. Other effects observed in horses include idiosyncratic neurological reactions consisting of behavior changes, gait abnormalities, and hyperesthesia. These effects improved soon after discontinuing the medication. Adverse effects associated with sulfonamides administered to dogs include allergic reactions, Type II and Type III hypersensitivity, arthropathy, anemia, thrombocytopenia, hepatopathy, keratoconjunctivitis sicca, and skin reactions. Dogs may be more sensitive to sulfonamides than other animals because dogs lack the ability to acetylate sulfonamides to metabolites and higher levels of more toxic metabolites. More descriptions of adverse reactions from sulfonamides are listed for individual drugs. Trimethoprim + sulfonamides may decrease thyroid hormone after treatment in dogs. Effects on thyroid function are most apparent after 2 weeks of treatment, but they are reversible.

### Contraindications and Precautions

Do not administer in animals with sensitivity to sulfonamides. Doberman pinschers may be more sensitive than other canine breeds to reactions from sulfonamides. Use cautiously in this breed. The injectable preparation contains benzyl alcohol, which may cause reactions in small patients. The injectable preparation should be diluted and injected slowly intravenously.

### Drug Interactions

Sulfonamides may interact with other drugs, including warfarin, methenamine, dapsone, and etodolac. They may potentiate adverse effects caused by methotrexate and pyrimethamine. Sulfonamides will increase metabolism of cyclosporine, resulting in decreased plasma concentrations. Methenamine is metabolized to formaldehyde, which may form a complex and precipitate with sulfonamides. Sulfonamides administered to horses that are receiving detomidine may develop cardiac arrhythmias. This precaution is only listed for IV forms of trimethoprim + sulfonamides.

## Instructions for Use

The dose listed is of the combined components: 30 mg/kg = 5 mg/kg trimethoprim and 25 mg sulfonamide. There is evidence that 30 mg/kg/day is efficacious for pyoderma; for other infections, 30 mg/kg twice daily has been recommended. When using the injectable formulation, each 5-mL vial should be diluted in 75-125 mL of 5% dextrose. The diluted formulation should then be administered by IV infusion over 60 minutes.

## Patient Monitoring and Laboratory Tests

Culture and susceptibility testing: All susceptibility testing is based on a 1:19 ratio of trimethoprim:sulfonamide. CLSI break point for susceptible organisms is  $\leq 2/38$  mcg/mL. For streptococci, this break point is  $\leq 2/38$  mcg/mL. Values



## 822 **Tripelennamine Citrate and Tripelennamine Hydrochloride**

listed are the concentration of trimethoprim + sulfonamide ratio. In dogs, trimethoprim + sulfadiazine may cause a functional hypothyroidism and lower total T<sub>4</sub> concentrations. Trimethoprim + sulfamethoxazole decreased thyroid function at 30 mg/kg q12h and at 15 mg/kg q12h. Trimethoprim + sulfadiazine at 15 mg/kg q12h for 4 weeks did not affect thyroid function in one study. Effects of trimethoprim + sulfonamides on thyroid function in dogs are reversible. In horses, trimethoprim + sulfadiazine did not affect assays of thyroid function.

### **Formulations**

- Trimethoprim + sulfamethoxazole is available in 480- and 960-mg tablets and a 240-mg/5 mL oral suspension (all formulations have a ratio of 5:1 sulfamethoxazole to trimethoprim).
- As an injection, it is available as 80 mg sulfamethoxazole and 16 mg trimethoprim per milliliter in 5-mL vials.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Injectable formulations should be stored at room temperature and not refrigerated. Injectable formulation contains 0.3% sodium hydroxide.

### **Small Animal Dosage**

#### **Dogs and Cats**

- Doses are listed as the combined sulfonamide + trimethoprim.
- 15 mg/kg q12h PO or 30 mg/kg q12-24h PO.
- 30 mg/kg q12h IV (see “[Instructions for Use](#)” section for preparation of IV formulation).

### **Large Animal Dosage**

#### **Horses**

- 30 mg/kg (25 mg sulfonamide + 5 mg trimethoprim) q12h PO for acute treatment. For some infections, treatment once a day at 30 mg/kg may be sufficient.

#### **Cattle**

- No dose is established. Trimethoprim is not absorbed orally in ruminants, but it is absorbed in calves. Trimethoprim + sulfadoxine has been used in cattle (16 mg/kg combined drug every 24 hours IV or IM), but this drug is not available in the US.

### **Regulatory Information**

Extralabel use of sulfonamides is prohibited from use in lactating dairy cattle. However, trimethoprim + sulfadoxine has a withdrawal time in Canada for cattle of 10 days for meat and 96 hours for milk.

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## **Tripelennamine Citrate and Tripelennamine Hydrochloride**

tri-peh-len'eh-meen sih'trate

**Trade and other names:** Pelamine, Histanin, and PBZ

**Functional classification:** Antihistamine

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### **Pharmacology and Mechanism of Action**

Antihistamine (H<sub>1</sub>-blocker). Similar to other antihistamines, tripelennamine acts by blocking the histamine Type 1 receptor (H<sub>1</sub>) and suppresses inflammatory reactions

caused by histamine. The H<sub>1</sub>-blockers have been used to control pruritus and skin inflammation in dogs and cats; however, success rates in dogs have not been high. More commonly used antihistamines include clemastine, chlorpheniramine, diphenhydramine, cetirizine, and hydroxyzine.

## Indications and Clinical Uses

Tripeennamine is used to prevent allergic reactions and for pruritus therapy in dogs and cats. In large animals, tripeennamine hydrochloride is used to treat laminitis, allergy, insect bites, pulmonary edema, and urticaria in horses. In cattle, it is used to treat urticaria and allergic reactions. Use in animals has been primarily derived from empirical use and experience in humans. Success rates for treatment of pruritus are low. In addition to the antihistamine effect for treating allergies, these drugs block the effect of histamine in the vomiting center, vestibular center, and other centers that control vomiting in animals.

## Precautionary Information

### Adverse Reactions and Side Effects

Sedation is the most common side effect. Antimuscarinic effects (atropine-like effects) also are common. Members of this class (ethanolamines) have greater antimuscarinic effects than other antihistamines. Gastrointestinal adverse effects may occur, such as ileus and decreased stomach emptying.

### Contraindications and Precautions

No contraindications are reported for animals.

### Drug Interactions

No drug interactions are reported for animals.

## Instructions for Use

There are no clinical reports of use in veterinary medicine, and no evidence that it is more efficacious than other drugs in this class.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Tripeennamine is available in 25- and 50-mg tablets, 20-mg/mL injections (generic), and 5-mg/mL elixir oral liquid. Tripeennamine hydrochloride (Histanin) is available as a 25-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- The dose is not clearly established. It has been listed as 1 mg/kg q12h PO. In humans, the dose is 1.25 mg/kg q4-6h PO. Tripeennamine hydrochloride injection: 0.25 mL per 5 kg body weight.

## Large Animal Dosage

- Pigs, cattle, and horses: 1 mg/kg IM, every 6-12 hours. Equivalent to 10 mL per 250 kg, or 1 mL per 25 kg body weight.

## Regulatory Information

Withdrawal time: Pigs and cattle: 48 hours for meat; 48 hours for milk.

RCI Classification: 3

## Tulathromycin

too-lath-roe-mye'sin

**Trade and other names:** Draxxin, and Draxxin 25

**Functional classification:** Antibacterial, Macrolide

### Pharmacology and Mechanism of Action

Antibacterial of the macrolide class of drugs. It is a 15-membered macrolide structure (gamithromycin also is a 16-member molecule) and considered a triamilide macrolide with three charged nitrogens. It is derived from azalide macrolides, such as azithromycin. Like other macrolides, it inhibits bacterial protein synthesis by binding to the ribosomal 50S subunit. It is considered bacteriostatic, but it may have bactericidal properties in vitro. Because of a positively charged molecule, it may penetrate gram-negative bacteria more easily than other macrolide antibiotics. Tulathromycin has a spectrum of activity that is limited to gram-positive bacteria and some gram-negative bacteria that cause respiratory diseases in cattle and pigs (e.g., *Mannheimia haemolytica*, *Mycoplasma*, and *Pasteurella multocida*). The half-life is long, with 80- to 90-hour plasma half-life in pigs and cattle, and 8- and 6-day tissue half-life in cattle and pigs, respectively, which prolongs the drug concentration at the site of infection. The volume of distribution is over 10 L/kg. Absorption from injection is over 80% in cattle and pigs.

Tulathromycin, like other macrolides, exerts therapeutic benefits not solely explainable by antibacterial activity. Like azithromycin, tulathromycin may have multiple immunomodulatory effects that likely contribute to the therapeutic response in respiratory infections, and perhaps other diseases. Other beneficial effects may be caused by enhanced degranulation and apoptosis of neutrophils and inhibition of inflammatory cytokine production. It also may help clear infections by enhancing macrophage functions.

### Indications and Clinical Uses

In cattle, tulathromycin is used for treatment of BRD caused by *M. haemolytica*, *P. multocida*, and *Histophilus somni* (formerly *Haemophilus somnus*). It is also effective for treating infections caused by *Mycoplasma bovis*. It also has been used to prevent infections caused by these pathogens when used in high-risk calves. It is also used for the treatment of bovine foot rot (interdigital necrobacillosis) associated with *Fusobacterium necrophorum* and *Porphyromonas levii*. A single dose has been effective for bovine infectious keratoconjunctivitis (*Moraxella bovis*).

In pigs, it has been used for control and treatment of SRD associated with *Actinobacillus pleuropneumoniae*, *P. multocida*, *Bordetella bronchiseptica*, *Mycoplasma hyopneumoniae*, and *Haemophilus parasuis*. In foals (extralabel use), tulathromycin has been used for treatment of pulmonary abscesses.

Other long-acting macrolide antibiotics used in cattle include tilmicosin, tildipirosin, and gamithromycin.

### Precautionary Information

#### Adverse Reactions and Side Effects

Serious adverse reactions have not been observed, except in experimental animals at high doses. Injection-site reactions are possible in some animals with swelling or irritation at the injection site. High doses (five times the dose) produced myocardial lesions in some animals. However, most animals have tolerated up to

10 times the labeled dose without toxicity. In treated foals (IM injection once per week) self-limiting diarrhea and injection site reactions (IM injection) developed in approximately one third of the foals.

It is ordinarily not administered to dogs, but in toxicity tests performed in dogs, it did not produce significant toxicity unless high doses were administered. There were no drug-related effects on heart rate, respiration rate, body temperature, blood pressure, or electrocardiographic parameters in dogs, even at high doses.

### **Contraindications and Precautions**

In cattle, do not administer to female dairy cattle 20 months of age or older. In cattle, do not inject more than 10 mL per injection site. In pigs, do not inject more than 2.5 mL per injection site.

### **Drug Interactions**

No drug interactions have been reported. However, macrolide antibiotics are known to inhibit some cytochrome P450 enzymes.

## **Instructions for Use**

In cattle, administer as a single SQ injection in the neck. In pigs, administer as a single IM injection in the neck.

## **Patient Monitoring and Laboratory Tests**

CLSI break point for susceptibility is  $\leq 16.0$  mcg/mL. For susceptibility testing, also use erythromycin as a guide.

## **Formulations**

Tulathromycin is available in a 25-mg/mL and 100-mg/mL solution for injection.

## **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

## **Small Animal Dosage**

- No small animal doses have been established.

## **Large Animal Dosage**

### **Cattle**

- 2.5 mg/kg SQ (neck) as a single injection (1.1 mL per 100 pounds for 100-mg/mL solution).

### **Pigs**

- 2.5 mg/kg IM (neck) as a single injection.

### **Foals**

- 2.5 mg/kg IM once per week.

## **Regulatory Information**

No milk withdrawal times are established.

Do not use in female dairy cattle 20 months of age or older. Do not use in veal calves.

Cattle withdrawal time for meat: 18 days when using Draxxin 100 mg/mL; when using 25 mg/mL, the withdrawal time is 22 days.

Pig withdrawal time for meat: 5 days.

## Tylosin

tye'loe-sin

**Trade and other names:** Tylocine, Tylan, and tylosin tartrate**Functional classification:** Antibacterial, macrolide

### Pharmacology and Mechanism of Action

Tylosin is a 16-membered macrolide approved for therapy of a variety of infections in pigs, cattle, dogs, and poultry (see indications below). It is formulated as tylosin tartrate or tylosin phosphate. Like other macrolide antibiotics, tylosin inhibits bacteria by binding to the 50S ribosome and inhibiting protein synthesis. Spectrum of activity is limited primarily to gram-positive aerobic bacteria. *Clostridium* and *Campylobacter* are usually sensitive. The spectrum also includes the bacteria that cause BRD. *Escherichia coli* and *Salmonella* are resistant. In pigs, *Lawsonia intracellularis* is sensitive.

### Indications and Clinical Uses

In cattle, tylosin is used for treatment of BRD caused by *Mannheimia*, *Pasteurella multocida*, and *Histophilus somni* (formerly *Haemophilus somnus*). It is used for interdigital necrobacillosis (foot rot) in cattle caused by *Fusobacterium necrophorum* or *Bacteroides melaninogenicus*. In pigs, it is used for treatment of swine arthritis caused by *Mycoplasma hyosynoviae*, swine pneumonia caused by *Pasteurella* spp., swine erysipelas caused by *Erysipelothrix rhusiopathiae*, swine dysentery associated with *Serpulina* (*Treponema*) *hyodysenteriae*, and proliferative enteropathy caused by *L. intracellularis*. For treatment in pigs, it is also added to feed (Type A—medicated feed article) or drinking water. In small animals, it is used for gram-positive soft tissue and skin infections. However, the most common use in dogs is for treatment of diarrhea, referred to as *antibiotic-responsive diarrhea*, that has not responded to other treatments. The etiology of the diarrhea is not known but may be caused by *Clostridium* or *Camphylobacter*. For this use, the powdered formulation (swine formulation) is most often added to food daily for maintenance.

### Precautionary Information

#### Adverse Reactions and Side Effects

Tylosin may cause diarrhea in some animals. However, oral treatment for colitis in dogs has been administered for several months with safety. Skin reactions have been observed in pigs. Oral administration to horses has been fatal.

#### Contraindications and Precautions

Do not administer orally to rodents or rabbits. Do not administer to horses. Avoid IV administration. Do not inject more than 10 mL in one IM site to avoid local reactions.

#### Drug Interactions

Although other macrolides have been associated with inhibition of cytochrome P450 enzymes, no drug interactions have been reported for animals.

### Instructions for Use

Tylosin is used in pigs and cattle for controlling the diseases listed in the Indications section. It is rarely used in small animals for uses other than intestinal disease.

Powdered formulation (tylosin tartrate) has been administered on food for control of signs of colitis in dogs. Tablets are approved for treatment of colitis in Canada.

### Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

### Formulations

Tylosin is available in a soluble powder 100 g per pound, or approximately 3 grams per teaspoon (Tylosin-100 Type A—medicated premix). Tylosin tartrate is equal to 800 micrograms per gram of tylosin base. It also is available as a 50- and 200-mg/mL injection (with propylene glycol).

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- 7-15 mg/kg q12-24h PO.
- 8-11 mg/kg q12h IM.
- Colitis: 12-20 mg/kg q8h with food, then if there is a response, increase the interval to q12h and eventually to q24h. (20 mg/kg is approximately 1/8 teaspoon of tylosin phosphate, or Tylan for a 20-kg dog.)

#### Cats

- 7-15 mg/kg q12-24h PO.
- 8-11 mg/kg q12h IM.

### Large Animal Dosage

#### Swine

- Treatment of arthritis, erysipelas, and swine dysentery: 8.8 mg/kg q12h IM.

#### Cattle

- Pododermatitis and pneumonia: 17.6 mg/kg q24h IM.
- Swine: Medicated feed dose is administered at a dose of 22-220 g/kg (of the premix), with dose depending on the specific product. Consult package information.

### Regulatory Information

Pig withdrawal time for meat: 14 days.

Cattle withdrawal time for meat: 21 days.

Not to be used in lactating cattle.

## Urofollitropin

yoo-roe-fah'lih-troe-pin

**Trade and other names:** Metrodin, FSH, and Fertinex

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Urofollitropin contains follicle-stimulating hormone (FSH) and stimulates ovulation. In people it is used in combination with human chorionic gonadotropin (hCG) to stimulate ovulation.

### Indications and Clinical Uses

Although urofollitropin is used in people in combination with hCG to stimulate ovulation, the use in animals is not common.

### Precautionary Information

#### Adverse Reactions and Side Effects

Side effects have not been reported in animals. In people, thromboembolism or severe ovarian hyperstimulation syndrome has been reported. In humans, ovarian enlargement and ovarian cysts have been reported.

#### Contraindications and Precautions

Do not use in pregnant animals.

#### Drug Interactions

No drug interactions are reported for animals.

### Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals is extrapolated from the experience in people. Use in humans is followed by administration of hCG.

### Patient Monitoring and Laboratory Tests

Monitor estrogen and/or progesterone with treatment.

### Formulations

- Urofollitropin is available in 75 units per vial for injection.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

- Doses not established. However, the usual human dose is 75 units/day IM for 7 days. This may be increased to 150 units/day IM for an additional 7 days.

### Large Animal Dosage

- Doses not established. However, the usual human dose is 75 units/day IM for 7 days. This may be increased to 150 units/day IM for an additional 7 days.

### Regulatory Information

It is expected to pose little risk from residues in animals intended for food, and no withdrawal times are recommended.

## Ursodiol, Ursodeoxycholic Acid

er-soe-dye'ole, er-soe-dee-oks-ih-koe-lik ass'id

**Trade and other names:** Actigall, Urso

**Functional classification:** Laxative, choleretic

### Pharmacology and Mechanism of Action

Hydrophilic bile acid. Ursodiol has anticholelithic and choleretic properties. Ursodiol is the short name for ursodeoxycholic acid. This is a naturally occurring, water-soluble bile acid. Ursodiol, like other bile acids, can act as a choleretic and increase bile flow. In dogs, it may alter the pool of circulating bile acids, displacing the more hydrophobic bile acids or enhancing their secretion in liver and bile. By modulating the composition of biliary bile salts in favor of more hydrophilic bile salts, injury to the biliary epithelium, such as the cytotoxic potential of endogenous bile acids, is less likely than with hydrophobic bile salts. There is also evidence that for treating acute liver injury, it may have antioxidant properties.

### Indications and Clinical Uses

Ursodiol is used for treatment of liver diseases. It is used to treat primary biliary cirrhosis, cholestatic liver disorders, and chronic liver disease. Although experimental evidence exists for its benefit in dogs, there are no well-controlled clinical trials that demonstrate efficacy. In people, it has been used as a laxative and to prevent or treat gallstones. It has also been used to treat chronic constipation because it may increase water content of feces and stimulate colonic peristalsis.

### Precautionary Information

#### Adverse Reactions and Side Effects

Loose feces and pruritus are the most common problems in people. In animals, ursodiol may cause diarrhea. Adverse effects can be decreased by gradually increasing the dose over 1-2 weeks.

#### Contraindications and Precautions

No contraindications are reported for animals.

#### Drug Interactions

No drug interactions have been identified for animals. In people, it interferes with some cholesterol-lowering drugs.

### Instructions for Use

Results of clinical studies in animals have not been reported. Use in animals (and doses) is based on experience in people or anecdotal experience in animals. The optimum dose in people is 13-15 mg/kg per day PO. Once or twice daily is as effective as three to four times per day. Administer with meals.

### Patient Monitoring and Laboratory Tests

Monitor bile acids and hepatic enzymes during treatment to monitor effects.

### Formulations

- Ursodiol is available in 300-mg capsules and 250- or 500-mg tablets.



### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Suspensions have been prepared in vehicles for oral use and found to be stable for 35-60 days.

### **Small Animal Dosage**

#### **Dogs and Cats**

- 10-15 mg/kg q24h PO; animals with liver disease should receive 15 mg/kg.

### **Large Animal Dosage**

- No large animal doses are available.

### **Regulatory Information**

It is expected to pose little risk from residues in animals intended for food, and no withdrawal times are recommended.

## Valacyclovir

Val a SYE kloe veer

**Trade and other names:** Valtrex

**Functional classification:** Antiviral

### Pharmacology and Mechanism of Action

Antiviral drug. Valacyclovir is acyclovir complexed with an amino acid (L-valine) by an ester. Therefore valacyclovir is a prodrug converted to the active acyclovir. Acyclovir has antiviral activity against herpes virus. The action is related to the affinity for the enzyme thymidine kinase (TK). Once converted to acyclovir, it is phosphorylated by thymidine kinase to the monophosphate form. Acyclovir monophosphate accumulates in cells infected with herpes virus and is converted by guanylate cyclase to acyclovir diphosphate and subsequently to the triphosphate form, which is an inhibitor of viral DNA polymerase. This terminates viral enzyme activity. However, resistance among some virus forms is possible because of changes in TK or in the DNA polymerase. There are also differences in activity among various strains of equine herpes virus (EHV). Some are more susceptible than other strains. It has poor activity against the feline herpes virus, and it is not recommended for this treatment.

After administration of oral valacyclovir, the oral absorption was 26% or as high as 48% (depending on the study) with a peak concentration of 4.2 mcg/mL (20 mg/kg) or 5.26 mcg/mL (26.6 mg/kg).

Other drugs in this class include penciclovir and famciclovir; information can be found in other monographs.

### Indications and Clinical Uses

Valacyclovir is an antiviral drug converted to acyclovir; therefore it can be used for similar indications as acyclovir, but with better and more consistent oral absorption. Valacyclovir is used for treatment of various forms of herpes virus infection in humans. The use in animals is limited, but it also has been used to treat herpes virus infection in horses.

It has been administered orally to horses because oral absorption of acyclovir is insufficient. Acyclovir is able to inhibit replication of EHV-1 in vitro, and valacyclovir has been used for oral treatment of EHV-1.

The activity against feline herpes virus is poor, and it produces adverse effects; therefore it is not recommended for cats.

### Precautionary Information

#### Adverse Reactions and Side Effects

The most serious adverse effect in humans is acute renal insufficiency. This may be prevented by slow IV infusion and proper hydration. No adverse effects were identified in limited studies performed in horses. In cats, significant adverse effects have been observed, which included myelosuppression and kidney and liver injury, including fatal hepatic and renal necrosis.

#### Contraindications and Precautions

Do not administer to cats. Do not use in animals with compromised kidney function.

#### Drug Interactions

Do not use with other nephrotoxic drugs.

## 832 Valproic Acid, Valproate Sodium

### Instructions for Use

The doses listed in the dosage section are based on pharmacokinetic studies to achieve the optimal plasma drug concentration. They are not based on clinical studies of efficacy. Oral administration in horses is not affected by feeding.

### Patient Monitoring and Laboratory Tests

Monitor blood urea nitrogen (BUN) and creatinine during use. In horses, doses should be administered to maintain plasma concentrations above 0.3 mcg/mL.

### Formulations

- Valacyclovir is available in 500-mg and 1-gram tablets.

### Stability and Storage

Store tablets in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs

- Canine doses have not been determined.

#### Cats

- Do not administer to cats.

### Large Animal Dosage

#### Horses

- 27 mg/kg oral loading dose q8h for 2 days. This is followed by a maintenance dose of 18 mg/kg PO q12h for 7-14 days.

### Regulatory Information

Because of mutagenicity, it should not be administered to animals intended for food.

## Valproic Acid, Valproate Sodium

val-proe'ik ass'id, val'proe-ate soe'dee-um

**Trade and other names:** Depakene (valproic acid), Depakote (divalproex), and Epival (in Canada)

**Functional classification:** Anticonvulsant

### Pharmacology and Mechanism of Action

Anticonvulsant. Action is not known, but valproate may increase gamma aminobutyric acid (GABA) concentrations in the central nervous system (CNS). Both valproic acid and valproate sodium are used. Divalproex is composed of both valproic acid and sodium valproate. Equivalent oral doses of divalproex sodium and valproic acid deliver equivalent quantities of valproate ion.

### Indications and Clinical Uses

Valproate is used, usually in combination with phenobarbital, to treat refractory epilepsy in animals. Most use has been in dogs, but limited efficacy studies have been reported. The use of valproate in animals has declined because other anticonvulsants for treating refractory epilepsy have been identified such as gabapentin, pregabalin, zonisamide, and levetiracetam.

## Precautionary Information

### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals, but hepatic failure has been reported in people. Sedation may be seen in some animals.

### Contraindications and Precautions

Do not use in pregnant animals. Birth defects have been reported in people.

### Drug Interactions

Valproate may cause bleeding if used with drugs that inhibit platelets.

## Instructions for Use

This drug is usually used as an add-on with phenobarbital. Controlled-release forms designed for people do not show the same oral absorption profile in dogs as in people.

## Patient Monitoring and Laboratory Tests

Therapeutic drug monitoring can be performed; however, therapeutic concentrations have not been established for dogs and cats, and ranges cited for people—50-100 mcg/mL (desired trough concentration)—should be used. Concentrations greater than 100 mcg/mL are associated with adverse effects.

## Formulations

- Valproic acid immediate-release formulations are available in 250-mg capsules and 50-mg/mL syrup. Delayed-release formulations of valproic acid and divalproex are available in 125-, 250-, and 500-mg tablets or capsules. Divalproex is also available in 125-mg capsules and 250- and 500-mg extended-release tablets. Valproate sodium (Depacon) is available in 100-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Valproic acid is slightly soluble in water, but valproate sodium is soluble in water. Extemporaneous emulsions have been prepared and were comparable to absorption of syrup.

## Small Animal Dosage

### Dogs

- 50-250 mg per dog (depending on size) q8h PO.
- Delayed-release formulations: Start with 250 mg per dog q12h PO and increase to 500 mg per dog q12h as needed.
- Higher doses should be used if dogs are also receiving phenobarbital.

### Cats

- Dose not established.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

## Vancomycin

van-koe-mye'sin

**Trade and other names:** Vancocin and Vancoled**Functional classification:** Antibacterial

### Pharmacology and Mechanism of Action

Antibacterial drug. Vancomycin is a glycopeptide antibiotic derived from a fungus *Amycolatopsis orientalis* (formerly *Nocardia orientalis*). Vancomycin is bactericidal for most organisms and bacteriostatic for enterococci. It inhibits the cell wall by binding to the D-alanyl-D-allanine portion of cell wall precursors and interfering with the bacterial cell wall. The bactericidal action occurs by activating bacterial cell wall autolysins. Vancomycin has a narrow antibacterial spectrum that includes *Streptococcus*, *Enterococcus*, and *Staphylococcus*. Strains of *Staphylococcus* treated often are called methicillin-resistant *Staphylococcus* (e.g., methicillin-resistant *Staphylococcus aureus* [MRSA] or *Staphylococcus pseudintermedius* [MRSP]). Gram-negative bacteria are resistant to vancomycin.

New drugs for humans related to vancomycin are dalbavancin (Dalvance), oritavancin (Orbactiv), and telavancin (Vibativ). These drugs are lipoglycopeptides. Oritavancin and dalbavancin are unique because they have very long half-lives of 10-14 days in people and can be administered once per 7-14 days. At this time, these new agents are very expensive and have not been tested for clinical use in animals.

### Indications and Clinical Uses

Vancomycin is used for resistant strains of *Staphylococcus* or *Enterococcus* in animals. It is commonly used in people as an injectable drug to treat methicillin-resistant *Staphylococcus* spp. and drug-resistant *Enterococcus* spp. It is not effective against gram-negative bacteria. However, it is used much less often in animals because it is inconvenient to administer and some countries have placed restrictions on use in animals. However, it can be valuable for treatment of enterococci or staphylococci that are resistant to other antibiotics when other options are not available. It has been administered orally to people for diarrhea caused by *Clostridium* spp., but this use has not been explored in animals. Occasionally it has been used in horses for local infiltration, such as with regional limb perfusion. It is not allowed in food animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported in animals, but the use has been limited to a small number of animals, and a full range of possible adverse effects has not been recognized. Adverse effects in people include neutropenia, kidney injury, and histamine release. Reactions, especially those associated with histamine release, are more likely with a rapid IV injection. The kidney injury is probably not relevant with the formulations used today because this was a reaction mostly caused by older, less pure formulations.

#### Contraindications and Precautions

Do not administer rapidly intravenously. It will cause pain if injected by other routes (IM, SQ). Administer by slow infusion to avoid acute adverse reactions.

#### Drug Interactions

Do not mix with other drugs in infusion solution; incompatibilities are identified for many drugs. Incompatible drugs include beta-lactam antibiotics, fluoroquinolones, aminoglycosides, macrolides, propofol, anticonvulsants, corticosteroids, and furosemide. It is incompatible with alkaline solutions.

## Instructions for Use

Vancomycin must be administered via IV infusion, although in rare instances intraperitoneal administration has been used in people. (Oral administration is limited to intestinal infections.) Vancomycin systemic use in horses is rare. Local administration in horses via regional limb perfusion has been used for localized joint or bone infections.

Doses are derived from pharmacokinetic studies in each species. In dogs, to maintain the plasma concentration between a suggested range of 10 and 30 mcg/mL, the dose rate of 15 mg/kg q8h IV is recommended. (This dose actually produces peaks and troughs of approximately 40 and 5 mcg/mL, respectively, but it is the most convenient dose that can be used because of the short half-life in dogs.) This dose should be infused slowly over 30-60 minutes, or at a rate of approximately 10 mg/min. The total dose to be administered can be diluted in 0.9% saline or 5% dextrose solution but not alkalizing solutions.

## Patient Monitoring and Laboratory Tests

Monitoring of trough plasma concentrations is recommended to ensure proper dose. Maintain trough concentration above 10 mcg/mL. Clinical and Laboratory Standards Institute (CLSI) guidelines for susceptibility testing list a break point of  $\leq 4$  mcg/mL for *Enterococcus*,  $\leq 1$  mcg/mL for *Streptococcus*, and  $\leq 2$  mcg/mL for *Staphylococcus*.

## Formulations

- Vancomycin is available in 500-mg and 1-, 5-, and 10-g vials for injection.

## Stability and Storage

Stability may be compromised if mixed with other drugs in infusion solutions. Store in a tightly sealed container, protected from light, and at room temperature. It is soluble in water and ethanol. After reconstitution with sterile water, it may be further diluted in 5% dextrose or saline. Solutions may have a dark color. After reconstitution, it is stable for 14 days either at room temperature or in the refrigerator. A concentrated solution of up to 83 grams/L was stable for 72 hours at 37° C. Some ophthalmic compounded formulations are not stable and have a low pH that can be irritating to the eyes.

## Small Animal Dosage

### Dogs

- 15 mg/kg q6-8h IV infusion.
- Constant-rate infusion (CRI): Loading dose of 3.5 mg/kg, followed by CRI of 1.5 mg/kg/hr mixed in 5% dextrose in water.

### Cats

- 12-15 mg/kg q8h IV infusion

## Large Animal Dosage

### Horses

- 4.3-7.5 mg/kg q8h IV given as an infusion over 1 hour.
- Regional limb perfusion: Infuse 300 mg diluted in a 0.5% solution.

## Regulatory Information

Do not administer to animals intended for food. The Food and Drug Administration (FDA) has prohibited the extralabel use of glycopeptides in food-producing animals because of risk of producing glycopeptide-resistant bacteria.

## Vasopressin

vay-zoe-press'in

**Trade and other names:** Arginine vasopressin (AVP), antidiuretic hormone (ADH), Pitressin

**Functional classification:** Hormone

### Pharmacology and Mechanism of Action

Antidiuretic hormone. Vasopressin mimics the effect of antidiuretic hormone (ADH) on the receptors of the renal tubule. Antidiuretic hormone permits reabsorption of water in the renal tubule. Without ADH, more diluted urine is excreted. (See desmopressin monograph for additional formulations and use.) Vasopressin also has potent vasopressive activity via activation of the  $V_1$  vascular receptor. The  $V_1$  vascular receptors are in high density on vascular smooth muscle, whereas it is the  $V_2$  receptors on the renal-collecting duct that are responsible for increasing water reabsorption. Because of the vasopressive action, it has been used to treat vasodilatory shock. During infusion it rapidly increases mean arterial pressure. A related drug, terlipressin, is more specific for the vascular  $V_1$  receptor.

### Indications and Clinical Uses

Vasopressin is used for treatment of polyuria caused by central diabetes insipidus. It is not effective for polyuria caused by renal disease. Desmopressin is the preferred formulation used more frequently in animals for treating diabetes insipidus (see desmopressin monograph in this book for more details.) Vasopressin is used to treat vasodilatory shock via CRI in addition to fluid therapy. In shock caused by cardiogenic mechanisms or vasodilatory shock, protocols vary with respect to the vasopressor used in emergency situations. Some protocols still rely on catecholamines (e.g., norepinephrine) for their vasoconstrictive properties (via  $\alpha_1$ -adrenergic receptors), and some protocols advocate vasopressin. There are no clinical trials in veterinary medicine that establish a superiority of one treatment over another.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects have not been reported for the use in animals. Allergic reactions and increase in blood pressure have been reported in people.

#### Contraindications and Precautions

No contraindications are reported for animals.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

For IV use, dilute in 0.9% saline and titrate dose to effect. For antidiuretic use, doses are adjusted on the basis of monitoring of water intake and urine output.

### Patient Monitoring and Laboratory Tests

Monitor blood pressure during infusion to maintain systolic blood pressure of 100-120 mm Hg and urine output of 0.5-1.5 mL/kg/hr. Titrate infusion rate to achieve desired pressure response. When used for antidiuretic effects, monitor water intake, urine output, and urine-specific gravity.

### Formulations

- Vasopressin is available in 20-units/mL (aqueous) solution.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- Antidiuretic: 10 units IV or IM.
- Vasopressor (shock): 0.01-0.04 units/min. Do not exceed 0.04 units/min. (0.5-5 milliunits/kg/min).
- CPR: 0.8 units/kg IV bolus; can be repeated during CPR.

### Large Animal Dosage

- No dose has been reported for large animals.

### Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Verapamil Hydrochloride

ver-ap'ah-mill hye-droe-klor'ide

**Trade and other names:** Calan and Isoptin

**Functional classification:** Calcium antagonist

### Pharmacology and Mechanism of Action

Calcium-channel blocking drug of the nondihydropyridine group. Verapamil blocks calcium entry into cells via blockade of the voltage-dependent slow channel. It produces vasodilation, negative chronotropic, and negative inotropic effects.

### Indications and Clinical Uses

Verapamil has been used to control supraventricular arrhythmias. The use of verapamil has diminished because of adverse effects; it has practically become an outdated drug. The preferred drug from this class to use in animals is usually diltiazem.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects include hypotension, cardiac depression, bradycardia, and AV block. It may cause anorexia in some patients. Verapamil has caused sudden cardiac arrest in some patients with IV administration.

#### Contraindications and Precautions

Do not use in patients with decompensated congestive heart failure (CHF) or advanced heart block. It is not well tolerated in cats.

#### Drug Interactions

Verapamil, like other calcium-channel-blocking drugs, is subject to interaction with drugs that interfere with the multidrug resistance (MDR) membrane pump (P-glycoprotein) and the cytochrome P450 enzymes. (See Appendixes I and J for a list of drugs that may cause interference.)



**Instructions for Use**

The oral formulation of verapamil is not absorbed sufficiently (of the active stereoisomer) for adequate effects. Diltiazem is preferred over verapamil in patients with heart failure because of less myocardial depression.

**Patient Monitoring and Laboratory Tests**

Monitor heart rate and rhythm during treatment.

**Formulations**

- Verapamil is available in 40-, 80-, and 120-mg tablets and a 2.5-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Verapamil is soluble in water. Aqueous solutions are stable for 3 months. Maximum stability is at pH 3-6. It can be mixed with infusion solutions and is compatible. Suspensions have been prepared for oral administration and found to be stable for 60 days.

**Small Animal Dosage****Dogs**

- 0.05 mg/kg q10-30min IV (maximum cumulative dose is 0.15 mg/kg).
- Oral dose is not established.

**Cats**

- Not recommended.

**Large Animal Dosage**

- No dose has been reported for large animals.

**Regulatory Information**

Do not administer to animals intended for food.

Racing Commissioners International (RCI) Classification: 4

**Vinblastine Sulfate**

vin-blast'een sul'fate

**Trade and other names:** Velban

**Functional classification:** Anticancer agent

**Pharmacology and Mechanism of Action**

Anticancer agent. Vinblastine, like vincristine, belongs to the vinca alkaloid group of anticancer agents. Vinblastine sulfate is the salt of an alkaloid derived from the *Vinca rosea* plant, also known as the Periwinkle flower. The vinca alkaloids have been called *spindle poisons* because they have an affinity for tubulin in cells. Tubulin is the protein that forms the microtubules responsible for chromosome migration during mitosis. Vinca alkaloids block polymerization of the cellular microtubules and therefore arrest mitosis in the metaphase (m-phase specific).

**Indications and Clinical Uses**

Vinblastine is used in cancer chemotherapy protocols for various tumors. One of the most common uses is for canine mast cell tumors (MCTs). There does not appear to be cross-resistance from vincristine to vinblastine. Vinblastine has been used for lymphoreticular neoplasia and also for canine transitional cell carcinoma and other tumors. Do not use vinblastine to increase platelet numbers as is done occasionally with vincristine. (Vinblastine may actually cause thrombocytopenia.)

## Precautionary Information

### Adverse Reactions and Side Effects

The most dose-limiting effect is bone marrow suppression, with the nadir of neutropenia occurring at 1 week after administration and recovery occurring at 2 weeks. Gastrointestinal toxicity is the second most important effect, but it is milder. Vinblastine does not produce neuropathy as vincristine does. It causes tissue necrosis if injected outside the vein.

### Contraindications and Precautions

If perivascular injection occurs, immediate flushing of area with fluids is recommended.

### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

Vinblastine may be used with other anticancer drugs or combined with prednisolone for MCTs. The most common dose has been 2 mg/m<sup>2</sup> every 7-14 days by slow IV infusion or rapid IV bolus. However, to increase the response rate for MCTs, evidence suggests that dose intensity should be increased to a dose of 3.5 mg/m<sup>2</sup> IV every 2 weeks. This dose produced more toxicity but higher efficacy.

## Patient Monitoring and Laboratory Tests

Monitor complete blood count (CBC) during treatment.

## Formulations

- Vinblastine is available in 1-mg/mL injection.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- 2 mg/m<sup>2</sup> IV (slow infusion) once/week. (See “Instructions for Use” regarding higher doses.)

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Vincristine Sulfate

vin-kris'steen sul'fate

**Trade and other names:** Oncovin, Vincasar, and generic brands

**Functional classification:** Anticancer agent

## Pharmacology and Mechanism of Action

Anticancer agent. Vincristine, like vinblastine, belongs to the vinca alkaloid group of anticancer agents. Vincristine is derived from the *Vinca rosea* plant, also known as

the Periwinkle flower. The vinca alkaloids have been called *spindle poisons* because they have an affinity for tubulin in cells. Tubulin is the protein that forms the microtubules responsible for chromosome migration during mitosis. Vinca alkaloids block polymerization of the cellular microtubules and therefore arrest mitosis in the metaphase (m-phase specific). Vincristine has an affinity for the tubulin of platelets. For thrombocytopenia, vincristine increases thrombopoiesis, increases fragmentation of megakaryocytes, and decreases platelet destruction. It may also decrease destruction of platelets by macrophages.

### **Indications and Clinical Uses**

Vincristine is used in combination chemotherapy protocols. It is included in several anticancer chemotherapy protocols, usually with corticosteroids, alkylating agents, and other drugs. It has been used in veterinary medicine for lymphoreticular tumors, transmissible venereal tumors (TVT), mammary neoplasia in cats, and other solid tumors. It is a component of several combination protocols and may also be useful as a single agent for some tumors.

### **Precautionary Information**

#### **Adverse Reactions and Side Effects**

Vincristine is generally well tolerated. It is less myelosuppressive than other anticancer drugs. Peripheral neuropathy has been reported, but it is rare. Constipation can occur. Vincristine is irritating to tissues; avoid extravasation outside the vein during administration. If accidental injection is made outside the vein, prompt action is needed to avoid severe tissue injury.

#### **Contraindications and Precautions**

If perivascular injection occurs, immediate flushing of the area with fluids is recommended to decrease tissue injury. When handling vincristine, pharmacy and hospital staff should take appropriate precautions to prevent exposure to people. Dogs with the ABCB-1 mutation (P-glycoprotein deficient) may have increased risk of toxicity.

#### **Drug Interactions**

There are no significant drug interactions.

### **Instructions for Use**

Vincristine is used in cancer chemotherapy protocols for various tumors. For example, in the COAP protocol (an acronym for cyclophosphamide, oncovin, asparaginase, and prednisolone), the oncovin component is vincristine. Vincristine also increases numbers of functional circulating platelets and is used for thrombocytopenia. When used to treat immune-mediated thrombocytopenia, it may be administered with a corticosteroid (e.g., prednisone at 2 mg/kg) to produce a rapid increase in functional platelets. This regimen (compared to prednisone alone) has shortened the duration of hospitalization for dogs with immune-mediated thrombocytopenia.

### **Patient Monitoring and Laboratory Tests**

Monitor platelets during therapy if used to increase platelet numbers.

### **Formulations**

- Vincristine is available in 1-mg/mL injection.

### **Stability and Storage**

Maintain in the injectable vial. Do not mix with other drugs in vial.

## Small Animal Dosage

### Dogs and Cats

- Antitumor: 0.5-0.75 mg/m<sup>2</sup> IV (or 0.025-0.05 mg/kg) once/week.
- Thrombocytopenia: 0.02 mg/kg IV once/week (with prednisolone).

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Withdrawal times are not established for animals that produce food. This drug should not be used in animals intended for food because it is an anticancer agent.

## Vitamin A

**Trade and other names:** Retinol, Aquasol-A, vitamin AD, and vitamins A and D

**Functional classification:** Vitamin

## Pharmacology and Mechanism of Action

Vitamin A supplement. See also isotretinoin (Accutane) for analogues used for other conditions.

## Indications and Clinical Uses

Vitamin A is used as a supplement for animals with deficiency.

## Precautionary Information

### Adverse Reactions and Side Effects

Excessive doses can cause bone or joint pain and dermatitis. Other signs of hypervitaminosis A can be excessive bleeding, confusion, diarrhea, and peeling of skin.

### Contraindications and Precautions

Hypervitaminosis A can occur from high doses of vitamin A administered chronically. Doses needed to cause toxicity can be as high as 10,000 units/kg/day.

### Drug Interactions

No drug interactions have been reported in animals.

## Instructions for Use

Dosing of vitamin A may be expressed as units, retinol equivalents (RE), or mcg of retinol. One RE equals 1 mcg of retinol. One RE of vitamin A is equal to 3.33 units of retinol. To convert from units of vitamin A to mcg, multiply units by 0.3. To convert from mcg vitamin A to units, divide by 0.3. (For example, 5000 units of vitamin A = 1500 mcg vitamin A.) One unit of vitamin A is equal to 0.6 mcg of beta-carotene.

## Patient Monitoring and Laboratory Tests

Monitor for signs of toxicity if high doses are used.

## Formulations

- Vitamin A is available in 5000 units (1500 RE) per 0.1 mL oral solution and in 10,000-, 25,000-, and 50,000-unit tablets. These tablets are listed as 3000, 7500, and 15,000 REs, respectively. Injectable formulations used in veterinary medicine usually are included with vitamin D. These combinations contain 100,000 units/mL, 200,000 units/mL, or 500,000 units/mL.

## Stability and Storage

Store protected from light at room temperature. Vitamin A, like other fat-soluble vitamins, is insoluble in water but soluble in oils. It is subject to oxidation and should be kept in a tightly sealed container.

## Small Animal Dosage

### Dogs and Cats

- 625-800 units/kg q24h PO.

## Large Animal Dosage

- All doses are listed as per animal and may be repeated in 2-3 months.

### Calves

- 500,000-1 million units IM.

### Sheep and Swine

- 500,000-1 million units IM.

### Cattle

- 1-2 million units IM.

## Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Vitamin E

**Trade and other names:** Tocopherol, alpha-tocopherol, Aquasol E, and generic brands

**Functional classification:** Vitamin

## Pharmacology and Mechanism of Action

Vitamin E is also known as *alpha-tocopherol*. It is a fat-soluble vitamin that is considered an antioxidant. Vitamin E also is found in solutions as d-alpha-tocopherol (natural source of vitamin E). It is often a component of omega fatty-acid formulations used in oral dietary supplements.

## Indications and Clinical Uses

Vitamin E is used as supplement and as treatment of some immune-mediated dermatoses and hepatobiliary disorders. Vitamin E has been used as an oral treatment for discoid lupus in dogs; however, efficacy for many skin diseases has been questioned. Vitamin E is often included in a mixture with other dietary supplements (e.g., fish oils).

## Precautionary Information

### Adverse Reactions and Side Effects

At high doses, vitamin E can cause coagulopathies. Doses known to cause coagulopathy are 1000 units/day (15 units/kg/day) in humans. Coagulopathies are caused by a decrease in vitamin K-dependent coagulation factors.

### Contraindications and Precautions

Use carefully in animals with coagulopathies.

### Drug Interactions

Vitamin E may interact with anticoagulants. It may exacerbate the anticoagulant effect of warfarin.

### Instructions for Use

Vitamin E has been proposed as treatment for a wide range of human illnesses, but evidence for efficacy in animals is lacking. In animals, it is used as adjunctive antioxidant therapy for a variety of diseases.

To convert to vitamin E if the product is labeled as DL-alpha-tocopherol: multiply units by 0.9 to determine mg. To convert from mg to units, divide by 0.9.

To convert to vitamin E if the product is labeled as D-alpha-tocopherol: multiply units by 0.67 to determine mg. To convert from mg to units, divide by 0.67. For example, 1 unit of vitamin A is equivalent to 0.67 mg d-alpha tocopherol or 0.9 mg dl-alpha tocopherol.

### Patient Monitoring and Laboratory Tests

Monitor for bleeding in animals treated with high doses.

### Formulations

- Vitamin E is available in capsules, tablets, and an oral solution (e.g., 1000 units/capsule). Injectable formulations for veterinary medicine may also contain vitamins A and D or selenium. Usually injectable combinations contain 300 units/mL. Vitamin E also is found in solutions as d-alpha-tocopherol (natural source of vitamin E). It is also often a component of omega fatty-acid (fish oils) formulations.

### Stability and Storage

Vitamin E, like other fat-soluble vitamins, is insoluble in water but soluble in oils. Store in a tightly sealed container, protected from light, and at room temperature.

### Small Animal Dosage

#### Dogs and Cats

- 100-400 units q12h PO (as alpha-tocopherol).
- Immune-mediated skin disease: 400-600 units q12h PO.
- Discoid lupus erythematosus (dogs): 200-400 units q12h PO.
- Liver disease: 10-15 units/kg/day, PO.

### Large Animal Dosage

- All doses are listed as per animal and may be repeated in 2-3 months.

#### Calves

- 1200-1800 units IM.

#### Cattle

- 2400-3000 units IM.

#### Sheep and Swine

- 1200-1800 units IM.

### Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Vitamin K

**Trade and other names:** Aquamephyton (injection), Mephyton (tablets), Veta-K1 (capsules), Veda-K1 (oral and injectable), vitamin K, phyloquinone, and phytomenadione

**Functional classification:** Vitamin

## Pharmacology and Mechanism of Action

See the phytonadione monograph in this book for additional information. Vitamin K is a cofactor used to synthesize coagulation factors in the liver (factors II, VII, IX, and X). Vitamin K-1 is also known as *phytonadione* and *phylloquinone* (phytomenadione is the British spelling of phytonadione). Vitamin K2 is also known as *menaquinone*. Vitamin K3 is known as *menadione*. Vitamin K3 is a synthetic analogue and is not equivalent to Vitamin K1. Vitamin K3 is not recommended for clinical use. Vitamin K1 is absorbed better with meals that contain fat.

## Indications and Clinical Uses

Vitamin K1 is a fat-soluble vitamin used to treat coagulopathies caused by anticoagulant toxicosis (warfarin or other rodenticides). Anticoagulants deplete vitamin K in the body, which is essential for synthesis of clotting factors. In large animals, it is used to treat sweet clover poisoning.

### Precautionary Information

#### Adverse Reactions and Side Effects

In people, a rare hypersensitivity-like reaction has been observed after rapid IV injection. This reaction may be caused by histamine release from a reaction from the drug vehicle polysorbate 80. Signs resemble anaphylactic shock. These signs also have been observed in animals. To avoid anaphylactic reactions, do not administer intravenously. Reactions from IM injection, such as hematoma, may occur in animals with coagulopathies.

#### Contraindications and Precautions

Accurate diagnosis to rule out other causes of bleeding is suggested. Other forms of vitamin K may not be as rapidly acting as vitamin K1; therefore consider using a specific preparation. To avoid anaphylactic reactions, do not administer intravenously.

#### Drug Interactions

Some drugs, such as cephalosporins, may decrease vitamin K-dependent clotting factors.

## Instructions for Use

Consult poison control center for specific protocol if specific rodenticide is identified. Use vitamin K1 for acute therapy because it is more highly bioavailable. Administer with food to enhance absorption. Phytonadione and phytomenadione are synthetic lipid-soluble forms of vitamin K1. Menadiol is vitamin K4, which is a water-soluble derivative converted in the body to vitamin K3 (menadione).

Injection can be diluted in 5% dextrose or 0.9% saline but not other solutions. Although vitamin K1 veterinary labels have listed the IV route for administration, these labels have not been approved by the FDA. Therefore avoid IV administration of vitamin K1. The preferred route is subcutaneous, but intramuscular also can be used. When treating for poisoning by second-generation rodenticides, which have long half-lives, 6 weeks of therapy may be necessary.

## Patient Monitoring and Laboratory Tests

Monitoring bleeding times in patients is essential for accurate dosing of vitamin K1 preparations. When treating long-acting rodenticide poisoning, periodic monitoring of the bleeding times is suggested.

## Formulations

- Vitamin K is available in 2- or 10-mg/mL injection. Mephyton is a 5-mg tablet. Veta-K1 is a 25-mg capsule. Phytonadione (Aquamephyton) is a 2- or 10-mg/mL injection.

## Stability and Storage

Vitamin K, like other fat-soluble vitamins, is insoluble in water but soluble in oils. Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- Short-acting rodenticides: 1 mg/kg/day IM, SQ, or PO for 10-14 days.
- Long-acting rodenticides: 2.5-5 mg/kg/day IM, SQ, or PO for 3-4 weeks and up to 6 weeks.

### Birds

- 2.5-5 mg/kg q24h, SC, IM, or PO for 14-28 days.

## Large Animal Dosage

### Cattle, Calves, Horses, Sheep, and Goats

- 0.5-2.5 mg/kg SQ or IM.

## Regulatory Information

No meat or milk withdrawal time is necessary.

## Voriconazole

vor-ih-kahn'ah-zole

**Trade and other names:** Vfend

**Functional classification:** Antifungal

## Pharmacology and Mechanism of Action

Azole (triazole) antifungal drug. Voriconazole is a second-generation triazole antifungal drug. Similar to the other currently available azole and triazole antifungals, voriconazole inhibits the fungal cytochrome P450-dependent 14 alpha-sterol demethylase, which is essential for formation of ergosterol in the fungal cell wall. Voriconazole is similar in structure to fluconazole; however, it is more active and potent. Voriconazole is active against dermatophytes and systemic fungi, such as *Blastomyces*, *Histoplasma*, and *Coccidioides*. It also has activity against yeast, such as *Candida* and *Malassezia*. Voriconazole has greater activity against *Aspergillus* and *Fusarium* than other drugs of this class. Voriconazole is more lipophilic than fluconazole and more water soluble than itraconazole or ketoconazole, with intermediate protein binding. These properties provide good oral bioavailability and tissue distribution. Pharmacokinetics may be dose dependent and variable among animals. Experimental studies in dogs have shown rapid and complete absorption of the drug following oral administration.

Pharmacokinetics have been studied in dogs, cats, and horses. Oral absorption is higher than in most other drugs in this class. In horses, voriconazole was absorbed 92% and had a half-life of 13 hours. The oral half-life is much longer than the IV half-life in cats, producing accumulation with repeated administration to cats. The IV half-life is 12.4 hours with a volume of distribution of 1.3 hours. The oral half-life in



cats is 43 hours with a peak of 2.3 mcg/mL at a dose of 4-6 mg/kg. Oral tablets and oral suspension in cats are absorbed equally well. Because of the difference in half-life, the oral administration to cats produces higher blood concentrations than the IV route (by a factor of 2.6). In dogs, after oral administration of 6 mg/kg, the half-life was 3.1 hours ( $\pm 0.8$ ) and a peak concentration of 3 mcg/mL. After repeated doses, the metabolism may be induced in dogs, producing a shorter half-life.

### Indications and Clinical Uses

Voriconazole has been used to treat dermatophytes and systemic fungi, such as *Blastomyces*, *Histoplasma*, and *Coccidioides*. It has been used to treat infections caused by *Aspergillus* and *Fusarium*. The efficacy in humans for treating *Aspergillus* is better than with other oral antifungal drugs and comparable to amphotericin B. Penetration into the CNS and eye is high enough to treat infections in these areas. Most of the use in veterinary medicine has been empirical or extrapolated from the use in humans. Clinical experience in horses has used a dose of 2 mg/kg once-daily PO. However, research studies have showed that a dose of 4 mg/kg once daily PO or a dose of 3 mg/kg q12h PO produces adequate in-plasma and tissue concentrations (ocular tear film, cerebrospinal fluid [CSF], urine, epithelial lining fluid of the lung, and synovial fluid) for susceptible fungi, including *Aspergillus*. It has also been administered topically in horses for ocular fungal infections (using the IV 1% solution every 4 hours). Voriconazole also has been used in birds to control infections caused by *Aspergillus*.

### Precautionary Information

#### Adverse Reactions and Side Effects

Voriconazole has been associated with neurotoxicity in cats at doses of 10 mg/kg via an unknown mechanism. Some cats administered therapeutic doses exhibited CNS signs that resolved after discontinuation of the drug. These reactions have not been reported in other animals (dogs, horses, birds) treated with voriconazole. Cats also had signs of anorexia, ataxia, paresis, arrhythmias, and hypokalemia. In a study with lower dosages (4-6 mg/kg), it was generally tolerated much better, but miosis and hypersalivation were common effects in cats.

Although it is generally better tolerated than ketoconazole in most species, increased liver enzymes, neurologic adverse effects, and decreased appetite have been observed in some dogs. Vomiting and hepatotoxicity are more likely at high doses. In people, transient ocular problems (blurred vision, photophobia) also have been reported.

#### Contraindications and Precautions

Doses of 10 mg/kg have caused neurologic problems in cats. A lower dose of 2-3 mg/kg every other day may be safe if administered by repeated doses, but an evaluation of the long-term safety has not been conducted in cats. Use cautiously in any animal with signs of liver disease. Use cautiously in pregnant animals. At high doses in laboratory animals, drugs in this class have caused fetal abnormalities. Use the oral formulation rather than the IV form in animals with renal disease.

#### Drug Interactions

Voriconazole is a cytochrome P450 enzyme inhibitor. It may cause drug interactions because of inhibition of P450 enzymes. However, this inhibition is not expected to be as prominent as with ketoconazole.

### Instructions for Use

Doses of voriconazole are based on experimental studies in animals. Some uses in animals are based on empiricism or extrapolation from human literature. When used

intravenously, the 10-mg/mL solution should be further diluted with fluids to a concentration  $>5$  mg/mL and infused slowly. Intravenous solutions should be used immediately or stored in the refrigerator not longer than 24 hours. It is compatible with lactated Ringer's solution, 5% dextrose, or sodium chloride 0.9%. Do not mix IV solution with blood products or concentrated electrolytes.

### Patient Monitoring and Laboratory Tests

Monitor liver enzyme concentrations. Minimum inhibitory concentration values for susceptible fungi are usually  $>0.5$  mcg/mL. Although not commonly monitored, the recommended trough drug concentration is  $>1$  mcg/mL. To avoid adverse reactions, do not exceed a peak  $>4$ -6 mcg/mL.

### Formulations

- Voriconazole is available in 50- and 200-mg film-coated tablets, 40-mg/mL oral liquid suspension, and 200-mg (10 mg/mL) injection. The IV solution requires reconstitution to 10 mg/mL, then dilution to 5 mg/mL or less for CRI (3 mg/kg/hr for 1-2 hours). A variety of compounded forms have been prepared for animals: A drug suspension for animals has been prepared by mixing crushed tablets (200 mg) with 20 mL water and 60 mL Ora-Plus to make a suspension of 2.5 mg/mL. After mixing, this suspension retained the original strength for 17 days. A compounded mixture also has been prepared by mixing two 200-mg tablets crushed to a powder and mixed with 10 mL of a suspending agent and flavoring agent (Ora Plus/Ora Sweet in a ratio of 1:1). The final formulation was 40 mg/mL and was stable for 30 days at room temperature or in the refrigerator. For horses, crushed tablets have been mixed with 30 mL of corn syrup and administered orally via syringe.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Compounded formulations may be stable and potent if used immediately after mixing. See “[Formulations](#)” section for stability information on compounded preparations. Use IV formulation immediately after mixing, or store in the refrigerator for not longer than 24 hours. Do not mix IV solutions with concentrated electrolytes or blood products.

### Small Animal Dosage

#### Dogs

- 5-6 mg/kg q12h PO. (Safety of repeated doses in dogs has not been examined.)

#### Cats

- Administer a loading dose of 25 mg per cat (range 4.2-4.6 mg/kg) PO, followed by 12.5 mg (2-2.3 mg/kg) every other day. Accumulation may occur after repeated doses; therefore observe for signs of adverse effects with multiple dosing.

#### Birds

- 10 mg/kg q12h PO administered as powder or crushed tablets mixed with water in a liquid suspension (0.5 mg/mL).

### Large Animal Dosage

#### Horses

- 2-4 mg/kg q24h or 3 mg/kg q12h PO.
- 1.5 mg/kg q24h IV.

### Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

## Warfarin Sodium

war'far-in soe'dee-um

**Trade and other names:** Coumadin and generic brands

**Functional classification:** Anticoagulant

### Pharmacology and Mechanism of Action

Anticoagulant. Warfarin sodium depletes vitamin K, which is responsible for generation of clotting factors. The half-life of warfarin in animals is 36-42 hours (20-30 hours in cats).

### Indications and Clinical Uses

In small animals, it has been used to treat hypercoagulation disease and prevent thromboembolism. In horses, warfarin has been used to treat navicular disease, although it is no longer popular for this use. The use of warfarin has diminished in small animals because it requires monitoring to optimize the dose, and because no clinical trials have shown efficacy for hypercoagulation states in animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

Adverse effects are attributable to decreased blood clotting. Spontaneous bleeding can result in blood loss, hemoperitoneum, hemarthrosis, gastrointestinal bleeding, epistaxis, and excessive bleeding from trauma or surgery.

#### Contraindications and Precautions

Do not administer to animals that may be prone to bleeding. Administer carefully with other drugs that are known to interfere with coagulation or with antiplatelet medications (e.g., aspirin or clopidogrel).

#### Drug Interactions

Multiple drugs and some foods may affect warfarin's action. Some of these that may potentiate warfarin's action include aspirin, chloramphenicol, phenylbutazone, ketoconazole, and cimetidine. Drug interactions are possible with administration with other highly protein-bound drugs, but such reactions are poorly documented in animals. Drug interactions are also possible with trimethoprim sulfonamides and metronidazole. Do not administer with some cephalosporin drugs (particularly those with N-methylthiotetrazole [NMTT]) because cephalosporins may induce bleeding through anti-vitamin-K-dependent mechanisms.

### Instructions for Use

Warfarin response can be highly variable among animals. Pharmacokinetic studies have attempted to correlate plasma pharmacokinetics with clinical response (prothrombin time [PT]). However, such a correlation has been difficult to demonstrate. A particular dose and plasma concentration that produces an effective prolongation of PT in one patient may not be effective in another individual. Because of the variation in response, adjust doses by monitoring bleeding times in treated animals. For a rapid effect, consider a loading dose of 6 mg per dog once daily for two treatments. Initial doses in cats have ranged from 0.06-0.09 mg/kg (0.25-0.5 mg/cat/day). When dividing tablets for treatment, it is best to crush up a whole tablet into a powder and divide the doses equally from the powder. When tablets are cut into halves or quarters, there may be uneven distribution of warfarin within the tablet. Some fractions of the tablet may contain a higher amount than others.

### Patient Monitoring and Laboratory Tests

Adjust dose by monitoring clotting time. Optimum dose is highly individualistic. The best method to monitor warfarin therapy is with the one-stage PT. Prothrombin times are reported in seconds and recorded as a ratio of the PT of the patient to the mean normal PT of the laboratory and as the international normalized ratio (INR). The INR is the most reliable way to monitor the PT. In animals, the dose is adjusted to maintain PT at 1.5-2 times normal (or INR of 2-3).

### Formulations

- Warfarin sodium is available in 1-, 2-, 2.5-, 4-, 5-, 7.5-, and 10-mg tablets.

### Stability and Storage

Warfarin sodium is soluble in water. It is light sensitive and should be packaged in tight containers. Solutions should have a pH >8 to maintain solubility. Some tablets do not have the drug distributed evenly; therefore uneven doses can result from splitting tablets.

### Small Animal Dosage

#### Dogs

- 0.1-0.2 mg/kg q24h PO. Start with this dose q12h for the first 2-4 days because of a lag time before maximum effect is observed.

#### Cats

- Start with 0.25-0.5 mg/cat/day and adjust dose based on bleeding time assessment.

### Large Animal Dosage

#### Horses

- 0.02 mg/kg q24h PO (9 mg per 450 kg of body weight [1000 pounds]). Increase this dose gradually by increments of 20% until a 2- to 4-second increase in PT bleeding time is achieved. Allow 7 days between changes in dose.

### Regulatory Information

Do not administer to animals intended for food.

Racing Commissioners International (RCI) Classification: 5

## Xylazine Hydrochloride

zye'lah-zeen hye-droe-klor'ide

**Trade and other names:** Rompun and generic brands

**Functional classification:** Alpha<sub>2</sub>-adrenergic agonist, analgesic, sedative

### Pharmacology and Mechanism of Action

Alpha<sub>2</sub>-adrenergic agonist. Alpha<sub>2</sub>-agonists decrease release of neurotransmitters from the neuron. They decrease transmission via binding to presynaptic alpha<sub>2</sub>-receptors (negative-feedback receptors). The result is decreased sympathetic outflow, analgesia, sedation, and anesthesia. Other drugs in this class include medetomidine, dexmedetomidine, romifidine, detomidine, and clonidine. Xylazine is not as specific as other drugs in this group. Receptor-binding studies indicate that alpha<sub>2</sub>/alpha<sub>1</sub>-adrenergic receptor selectivity was 1620 for medetomidine and 160 for xylazine.

### Indications and Clinical Uses

Xylazine is used for short-term sedation, anesthesia, and analgesia in horses, dogs, cats, cattle, and exotic animals. Like other alpha<sub>2</sub>-agonists, it is used as an anesthetic adjunct and analgesic. The duration of effect is approximately 30 minutes. Compared with xylazine, dexmedetomidine and medetomidine produce better sedation and analgesia in dogs. Romifidine produces the longest duration of sedative effects, followed by detomidine, medetomidine, and xylazine.

### Precautionary Information

#### Adverse Reactions and Side Effects

In small animals, vomiting is the most common acute effect, which is more prominent in cats than dogs. Xylazine produces sedation and ataxia. Xylazine, like other alpha<sub>2</sub>-agonists, decreases sympathetic output. Cardiovascular depression may occur. Cardiac effects can include sinoatrial block, first- and second-degree AV block, bradycardia, and sinus arrhythmia. In ruminants, use of xylazine may decrease gastrointestinal (GI) motility and cause bloating, salivation, and regurgitation. Note that cattle, sheep, and goats are much more sensitive to xylazine than other animals, which requires lowering the dose. Among horses, draft horses are more sensitive to the effects than thoroughbred and Arab horses. Like other alpha<sub>2</sub>-agonists, xylazine produces transient hyperglycemia, which may increase urine flow.

#### Contraindications and Precautions

Ruminants are much more sensitive to xylazine than other species, and lower doses must be used compared with other animals. Use cautiously in animals that are pregnant. Xylazine impairs blood flow to the uterus during gestation in cows and may decrease oxygen delivery to the fetus, especially in late gestation. Use caution when using xylazine to sedate pregnant cows. It also may induce labor. Use cautiously, if at all, in patients with cardiac disease. Because of cardiac depression, it should not ordinarily be used with tranquilizers such as phenothiazines.

#### Drug Interactions

Use with opioid analgesic drugs will greatly enhance the central nervous system (CNS) depression. Consider lowering doses if administered with opioids. Do not administer with other drugs that cause significant cardiac depression.

## Instructions for Use

Xylazine is often used in combination with other drugs (e.g., ketamine or butorphanol). It is combined with guaifenesin and ketamine in the equine “triple drip” combination (see [dosing section](#)).

It is not necessary to premedicate animals with atropine. For large animals, if sedation is needed without recumbency, use the lower end of the dose range. Reverse effects of xylazine with an  $\alpha_2$ -antagonist (e.g., yohimbine, tolazoline, or atipamezole) if adverse effects are serious enough to warrant reversal. Xylazine also may be administered intra-osseous to horses when it is not possible to give an IV injection. It is equally bioavailable from the intra-osseous route as IV.

## Patient Monitoring and Laboratory Tests

Monitor heart rate and rhythm during anesthesia with xylazine. It may cause increased plasma glucose in animals.

## Formulations Available

- Xylazine is available in 20- and 100-mg/mL injections.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs

- 1.1 mg/kg IV.
- 2.2 mg/kg IM.
- Short-term treatment of pain: 0.1-0.5 mg/kg IM, IV, or SQ.

### Cats

- 1.1 mg/kg IM.
- Emetic dose: 0.4-0.5 mg/kg IM, or IV.
- Short-term treatment of pain: 0.1-0.5 mg/kg IM, IV, or SQ.

## Large Animal Dosage

### Horses

- 1-2 mg/kg IM.
- Standing chemical restraint: 0.5-1.0 mg/kg IV bolus. (The intravenous dose also can be administered intra-osseous with equal bioavailability.)
- 0.5-1.1 mg/kg IV, followed by (if necessary) 0.72 mg/kg/hour constant-rate infusion (CRI).
- For colic pain: 0.3-0.5 mg/kg IV (150-250 mg IV for average-size horse).
- For anesthesia purposes, it is sometimes combined with other agents such as ketamine and guaifenesin in the equine “triple-drip” combination. This combination consists of 500 mg xylazine and 2 g ketamine added to 1 L of 5% guaifenesin in dextrose. It is administered at a rate of 1.1 mL/kg for induction, followed by 2-4 mL/kg/hour for maintenance. Recovery usually occurs in 25-30 minutes, or administer 0.125 mg/kg yohimbine to speed up recovery.

### Pigs

- 0.5-3 mg/kg IM. (Use in combination with other drugs in swine (e.g., 2 mg/kg xylazine + 10 mg/kg ketamine, administered IM). It is unreliable alone.)

### Cattle

- 0.1-0.2 mg/kg IM.
- 0.03-0.1 mg/kg IV.

## 852 **Xylazine Hydrochloride**

### **Sheep**

- 0.1-0.3 mg/kg IM.
- 0.05-0.1 mg/kg IV.

### **Goats**

- 0.05-0.5 mg/kg IM.
- 0.01-0.5 mg/kg IV.

### **Regulatory Information**

Withdrawal time for cattle: At doses of 0.016-0.1 mg/kg, 5 days for meat and 72 hours for milk. At doses of 0.05-0.3 mg/kg, 10 days for meat and 120 hours for milk. In Canada it is listed as 3 days for meat and 48 hours for milk, whereas in the UK it is listed as 14 days for meat and 48 hours for milk. (If yohimbine is used as reversal, use withdrawal time of 7 days for meat and 72 hours for milk.)

Racing Commissioners International (RCI) Classification: 3

## Yohimbine

yoe-him' been

**Trade and other names:** Yobine

**Functional classification:** Alpha<sub>2</sub>-receptor antagonist

### Pharmacology and Mechanism of Action

Alpha<sub>2</sub>-adrenergic antagonist. It is derived from several botanical sources (tree bark, roots, and other plants) and nonselectively antagonizes alpha-adrenergic receptors. It antagonizes the action of other drugs that stimulate the alpha<sub>2</sub>-receptor. At high doses, it may act as an agonist for other receptors such as the alpha<sub>1</sub>, dopamine, and serotonin receptor. Alpha<sub>2</sub>-agonists have profound effects on blood pressure, cardiac output, and intestinal motility, as well as their well-known properties of sedation and analgesia. The alpha<sub>2</sub>-antagonists such as yohimbine can reverse these effects when necessary.

In horses, when administered at 0.12 mg/kg, it has a half-life of approximately 4.4 hours and volume of distribution of 3.2 L/kg.

### Indications and Clinical Uses

Yohimbine is used primarily to reverse actions of xylazine or detomidine. Atipamezole is another alpha<sub>2</sub>-antagonist that is more specific and is preferred to use in small animals to reverse dexmedetomidine or medetomidine. Atipamezole is more specific for the alpha<sub>2</sub>-receptor. Tolazoline has also been used to reverse effects of xylazine in horses.

### Precautionary Information

#### Adverse Reactions and Side Effects

Yohimbine can produce a variety of responses in horses. Some horses show excitation rearing, striking, muscle tremors, and exaggerated response to stimuli. Yohimbine may cause more transient excitement than either atipamezole or tolazoline. It can produce cardiovascular events in horses such as increased heart rate.

High doses can cause tremors and seizures. If used alone (not recommended), it can produce a variety of undesirable events.

#### Contraindications and Precautions

When administering to reverse an alpha<sub>2</sub>-agonist, monitor heart rate and rhythm carefully during treatment. There is no therapeutic justification to administer an alpha<sub>2</sub>-antagonist such as yohimbine as a single agent to treat horses for any diseases.

#### Drug Interactions

Detomidine increases the plasma concentration and decreases clearance of yohimbine. No other interactions are reported, except the antagonism of alpha<sub>2</sub>-agonists.

### Instructions for Use

Reverses signs of sedation and anesthesia caused by alpha<sub>2</sub>-agonists. Because the drug concentrations of the alpha<sub>2</sub>-agonist may be diminished considerably by the time reversal becomes necessary in clinical practice, it may not be necessary to provide a full dose of yohimbine (or other alpha<sub>2</sub>-antagonist) because a full dose may induce excitement and other undesirable events. Instead, one third of the recommended dose of yohimbine can be administered first, followed by (if necessary) the same amount in 5- to 10-minute increments.



**Patient Monitoring and Laboratory Tests**

Monitor heart rate and rhythm during use of yohimbine.

**Formulations**

- Yohimbine is available in a 2-mg/mL injection.

**Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature.

**Small Animal Dosage****Dogs and Cats**

- 0.11 mg/kg IV.
- 0.25-0.5 mg/kg SQ or IM.

**Large Animal Dosage****Horses**

- 0.125 mg/kg IV (to reverse xylazine).
- 0.2 mg/kg IV (to reverse detomidine).
- Note about reversal: It may not be necessary to give the full dose initially. See [“Instructions for Use”](#) for more details.

**Cattle and Sheep**

- To reverse xylazine or medetomidine: 0.125-0.2 mg/kg IV.

**Regulatory Information**

Food animal withdrawal time: At least 7 days for meat and 72 hours for milk.

Racing Commissioners International (RCI) Classification: 2

## Zidovudine

zye-doe'vyoo-deen

**Trade and other names:** Retrovir

**Functional classification:** Antiviral

### Pharmacology and Mechanism of Action

Antiviral drug. Zidovudine (also known as *azidothymidine* or *AZT*) acts to inhibit the viral enzyme reverse transcriptase that prevents conversion of viral RNA into DNA. Other drugs in this class include lamivudine, didanosine, and zalcitabine.

### Indications and Clinical Uses

In people, AZT is used to treat HIV (AIDS). In animals, it has been experimentally used for treatment of feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) infection in cats. In cats, doses of 25 mg/kg q12h IV or PO produced drug concentrations in the effective range to inhibit the virus. In experimentally infected cats with FeLV, it was effective to improve clinical signs. However, in naturally infected cats, it has not been effective and the use in cats for this disease has been disappointing. In some cats, it may be more helpful for FIV than for FeLV and can improve quality of life, decrease virus load, and improve clinical signs in cats with FIV.

### Precautionary Information

#### Adverse Reactions and Side Effects

Anemia and leucopenia have been observed in treated animals. Adverse effects are more common in cats at high doses. It has not been used often in animals; therefore a full range of potential adverse effects has not been reported.

#### Contraindications and Precautions

No contraindications are reported for animals.

#### Drug Interactions

No drug interactions have been reported in animals.

### Instructions for Use

At this time, experience with using AZT for treating viral disease in animals is largely experimental or anecdotal. This drug may help some cats with FIV and may prevent persistent FeLV, but documentation of efficacy is lacking.

### Patient Monitoring and Laboratory Tests

Monitor the packed-cell volume (PCV) in treated cats and perform a complete blood count (CBC). This should be done once per week initially, then once per month after the cat is stabilized.

### Formulations

- AZT is available in a 10-mg/mL syrup and a 10-mg/mL injection. The syrup has been reformulated into capsules for cats.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Cats

- 5-10 mg/kg PO or SQ q12h. If administered SQ, dilute in saline first to avoid injection site irritation.

## Large Animal Dosage

- No dose has been reported for large animals.

## Regulatory Information

Do not administer to animals intended for food.

## Zilpaterol Hydrochloride

Zil-pat'-e-role

**Trade and other names:** Zilmax

**Functional classification:** Beta-adrenergic agonist

## Pharmacology and Mechanism of Action

Zilpaterol is a synthetic beta-receptor adrenergic agonist. It resembles other beta-agonists in some actions to produce effects similar to norepinephrine. Zilpaterol is administered to cattle in feed as a growth promotant and to improve feed efficiency. Zilpaterol, like other beta-adrenergic agonists, stimulates beta<sub>2</sub>-adrenergic receptors in muscle and promotes muscle gain with less fat. Subsequently, if fed to cattle at approved levels, zilpaterol increases feed efficiency and improves muscle weight gain. In clinical studies, it substantially increased skeletal muscle mass and cross-sectional area of individual muscles.

## Indications and Clinical Uses

Zilpaterol is fed to cattle (Type A medicated feed) to improve weight gain and muscle mass. It has been approved in the US and other countries for this use.

## Precautionary Information

### Adverse Reactions and Side Effects

Like other beta-adrenergic agonists, zilpaterol can produce cardiovascular problems associated with increased stimulation of receptors at high doses.

### Contraindications and Precautions

Severe adverse effects such as tachycardia, tremors, and muscle fasciculations have been observed in horses. Zilpaterol should not be administered to horses, and precautions should be taken to ensure that horses are not accidentally exposed to zilpaterol-treated cattle feed.

Because beta-adrenergic agonists such as clenbuterol are abused in humans for the purpose of promoting muscle gain and fat loss, there is a possibility that zilpaterol also could be abused in the same manner.

Labeling should include the following information: (1) Do not allow horses or other equines access to feed containing zilpaterol. (2) Not for use in animals intended for breeding. (3) Do not use in veal calves.

### Drug Interactions

Use caution when administering to animals receiving other adrenergic medications.

## Instructions for Use

Zilpaterol is used to increase rate of weight gain, improve feed efficiency, and increase carcass leanness in cattle fed in confinement for slaughter during the last 20-40 days on feed. It should be fed continuously as the sole ration during the last 20-40 days on feed.

## Patient Monitoring and Laboratory Tests

No specific monitoring is necessary.

## Formulations

- Type A medicated articles containing 21.77 g zilpaterol hydrochloride per pound.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

- No small animal dose is established. No established uses for small animals.

## Large Animal Dosage

- Do not administer to horses.
- Cattle dose: 6.8 g/ton of feed to provide 60-90 mg zilpaterol hydrochloride per head per day.

## Regulatory Information

Cattle withdrawal time for slaughter: 3 days. RCI Classification for horses: Class 3.

## Zinc

**Trade and other names:** Zinc

**Functional classification:** Nutritional supplement

## Pharmacology and Mechanism of Action

Zinc is an essential element important in more than 200 metalloenzymes. It also is important for nucleic acid, cell membrane, and protein synthesis. In addition, it is important for growth, tissue repair, and cell division. Zinc acts as a chelating agent, and it competes with iron to inhibit fibrosis and collagen formation. It induces the production of metallothionein in intestinal mucosal cells, which binds copper from the diet and prevents uptake to the liver. The benefits have been seen in experimental animals and in humans with liver disease. One of the uses has been to manage hepatic cirrhosis. Zinc also may act as an antioxidant and prevent membrane damage.

## Indications and Clinical Uses

It has been used to treat zinc-deficient diseases such as those that cause dermatologic problems. It is also used as an antifibrotic agent in liver disease. One of the other uses of zinc is as a chelating agent in animals. Most commonly, zinc has been used as a cupruritic to decrease copper concentrations in animals with liver disease, often in combination with other drugs (e.g., penicillamine). When used to treat copper liver disease, it is slow acting and may take as long as 3 months for the full effect.

## Precautionary Information

### Adverse Reactions and Side Effects

The most common effect is gastrointestinal (GI) problems, including nausea and vomiting. Hemolysis and anemia can be observed with high doses.

### Contraindications and Precautions

If IV forms are used (e.g., zinc sulfate), adverse effects may be more likely because ordinarily the oral absorption is more limited.

### Drug Interactions

Oral absorption is impaired from tetracyclines, iron, copper, phytates (found in bran and grains), and penicillamine.

## Instructions for Use

Administer without food to improve oral absorption, but a small meal will often prevent some of the nausea associated with treatment. When considering various forms, the gluconate form may be better tolerated than the sulfate or acetate form.

## Patient Monitoring and Laboratory Tests

Monitor blood zinc concentrations at least monthly to prevent high levels, which cause hemolysis. Blood zinc concentrations should ideally be 200-500 mcg/dL. A concentration above 800 mcg/dL is considered toxic, but levels above 200 mcg/dL are needed to treat copper liver disease.

## Formulations

- Zinc is available in several forms, including zinc sulfate (23% zinc), zinc gluconate (14% zinc), and zinc acetate (35% zinc). Zinc gluconate is available in tablets ranging from 1.4-52 mg (10 mg zinc gluconate = 1.4 mg of elemental zinc). Zinc sulfate is available in capsules containing 25 and 50 mg elemental zinc (110 mg zinc sulfate = 25 mg elemental zinc). Zinc sulfate is also available in tablets containing 15, 25, 45, and 50 mg elemental zinc (66 mg zinc sulfate = 15 mg elemental zinc). Injectable zinc sulfate is available in a 50-mg/mL (20.2 mg elemental zinc per mL) solution for IV use.

## Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature.

## Small Animal Dosage

### Dogs and Cats

- Adjust dose based on measuring plasma zinc concentrations.
- Hepatic disease in dogs: 100 mg elemental zinc per dog q12h PO, or 3 mg zinc gluconate/kg per day, or 2 mg zinc sulfate/kg per day PO. (Consider including vitamin E with treatment.)
- Zinc supplement: 1 mg/kg elemental zinc gluconate or sulfate three times/day PO, or 1.5-3 mg (of elemental zinc) zinc acetate daily per animal PO.
- Dermatologic use: 10 mg/kg daily (zinc sulfate or zinc gluconate).
- Intravenous zinc treatment: 50 mcg elemental zinc/kg infused IV slowly per day.

## Large Animal Dosage

- No specific doses have been reported. Extrapolate dose needed from small animal use (approximately 1 mg/kg elemental zinc three times per day PO) and adjust dose by monitoring zinc concentrations.

## Regulatory Information

Because of low risk of harmful residues in animals intended for food, no withdrawal time is suggested.

## Zoledronate

Zoe'-le-droe-nate

**Trade and other names:** Zometa, Zoledronic acid

**Functional classification:** Antihypercalcemic

## Pharmacology and Mechanism of Action

Bisphosphonate drug. Zoledronate is zoledronic acid (Zometa). Other drugs in this class include pamidronate, etidronate, tiludronate, clodronate, and alendronate. These drugs belong to a group characterized by a germinal aminobisphosphonate bond. They slow the formation and dissolution of hydroxyapatite crystals. These drugs are classified on the basis of whether they contain a nitrogen group. Zoledronate is a nitrogen-containing bisphosphonate, which has a hydroxyl group on carbon units opposite the nitrogen group that leads to slow metabolism and that is poorly metabolized and achieves high affinity for bone surfaces. Their clinical use resides in their ability to inhibit bone resorption. Inhibition of bone resorption is via inhibition of the mevalonate pathway. These drugs decrease bone turnover by inhibiting osteoclast activity, inducing osteoclast apoptosis, retarding bone resorption, and decreasing the rate of osteoporosis. In dogs, after infusion, the half-life was approximately 2.2 hours, with a volume of distribution of 0.28 L/kg.

## Indications and Clinical Uses

Zoledronate, like other bisphosphonate drugs, is used to treat refractory hypercalcemia, osteoporosis, and treatment of hypercalcemia of malignancy. In animals, bisphosphonates are helpful for managing neoplastic complications and pain associated with pathologic bone resorption. They also may provide pain relief in patients with pathologic bone disease. Other uses include osteoporosis and skeletal metastasis. It has been used in similar protocols as for pamidronate, but has the advantage of a 15-minute infusion IV rather than 2-4 hours for pamidronate. In horses, it has been administered via IV infusion for bone pain and conditions associated with bone fragility. In horses, it has a plasma half-life of 2.2 hours after IV administration, but persists in bone for much longer. Bisphosphonates that are approved for horses for treatment of navicular disease and other bone disorders include tiludronate and clodronate. See sections in this book for more information on these drugs for horses.

## Precautionary Information

### Adverse Reactions and Side Effects

Zoledronate may be safer than pamidronate. Fever, joint pain, and myalgias have been observed in people, but otherwise no serious adverse effects have been identified. The use in animals has not been common enough to identify a wider range of adverse effects. In people, there is some concern that the use of bisphosphonates produces excessive mineralization and hardening of the bone, which may result in a greater risk of fractures. However, this effect has not been reported for animals.

### Contraindications and Precautions

Do not administer during pregnancy.

**Drug Interactions**

Do not mix with calcium or other divalent cation-containing infusion solutions, such as lactated Ringer's solution. It should be administered as a single IV solution in a line separate from other drugs.

**Instructions for Use**

Zoledronate is intended for IV infusion. Dilute vial in 0.9% saline or 5% dextrose solution for IV use. If not used immediately after dilution, the solution should be refrigerated, and the refrigerated solution then should be equilibrated to room temperature prior to administration. The total time between dilution, storage in the refrigerator, and end of administration must not exceed 24 hours.

When administered to horses, monitor creatinine, blood urea nitrogen (BUN), and calcium prior to administration to ensure that it is safe for the patient. Calcium supplementation in the diet is recommended.

**Patient Monitoring and Laboratory Tests**

Monitor serum calcium and phosphorus. Monitor BUN, creatinine, urine-specific gravity, and food intake in treated animals.

**Formulations**

- Zoledronate is available in a 4-mg/5 mL vial for infusion.

**Stability and Storage**

Store in a vial at room temperature. Vials may be diluted in fluid solutions. Storage and stability information is listed in the "Instructions for Use" section.

**Small Animal Dosage****Dogs**

- 0.2-0.25 mg/kg IV infused over 15 minutes, diluted in 100 mL 0.9% saline (large dogs) or 50 mL 0.9% saline (small dogs). This dose can be administered once every 28 days.
- For osteoporosis: 5 mg (per dog) every 1-2 years IV.
- Hypercalcemia associated with cancer: 4 mg (per dog) infusion every 7 days.
- Multiple myeloma: 4 mg (per dog) infusion every 3-4 weeks.

**Cats**

- 0.2 mg/kg IV over 15 minutes diluted in a volume of 25 mL every 21-28 days.

**Large Animal Dosage****Horses**

- 0.075 mg/kg. Dissolve each dose in 50 mL of 11.3 mg/mL citrate solution, then mix with 500 mL (400 mL saline and 100 mL mannitol). Administer via IV infusion to horses over 15-30 minutes. Other bisphosphonates are approved for horses and include tiludronate and clodronate.

**Regulatory Information**

Withdrawal times are not established for animals that produce food. For extralabel use withdrawal interval estimates, contact Food Animal Residue Avoidance Databank (FARAD) at 1-888-USFARAD (1-888-873-2723).

## Zolpidem

Zole - PI - dem

**Trade and other names:** Ambien, Edluar, Intermezzo, Zolpimist

**Functional classification:** Sedative

### Pharmacology and Mechanism of Action

Sedative. Zolpidem is a nonbenzodiazepine sedative. In people, it has effects similar to the benzodiazepines and is used as a sedative and sleep aid.

Like benzodiazepines, zolpidem potentiates the action of gamma aminobutyric acid (GABA), an inhibitory neurotransmitter. However, it does not cause muscle relaxation or produce anticonvulsant properties. The benzodiazepines act on the GABA<sub>A</sub> and GABA<sub>B</sub> receptor. GABA<sub>A</sub> has omega-1, omega-2, and omega-3 receptors. Benzodiazepines act on all receptors, but zolpidem and other drugs known as *Z-drugs* only act on the omega-1 receptor to produce sedation.

### Indications and Clinical Uses

Zolpidem is used as a sedative and sleep aid in people. However, this property has not been shown in animals.

### Precautionary Information

#### Adverse Reactions and Side Effects

In dogs, it produced adverse effects that included vocalization, restlessness, anxiety, dysphoria, rage reaction, excitement, muscle spasticity, and hyperreflexia.

#### Contraindications and Precautions

Because of the adverse reactions observed, it is not recommended for dogs.

#### Drug Interactions

Avoid use with other sedatives, behavior-modifying drugs, or drugs that decrease drug metabolism.

### Instructions for Use

Clinical uses have not been established for veterinary patients.

### Patient Monitoring and Laboratory Tests

No monitoring has been recommended for animals.

### Formulations

- Available in 5- or 10- mg tablets.

### Stability and Storage

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### Small Animal Dosage

#### Dogs

- 0.5 mg or 0.15 mg/kg, once.

#### Cats

- Dose regimens have not been defined in cats.

### Large Animal Dosage

- No dose has been reported for large animals.



## Regulatory Information

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Schedule IV controlled substance

## Zonisamide

zoe-nis'a-mide

**Trade and other names:** Zonegran

**Functional classification:** Anticonvulsant

## Pharmacology and Mechanism of Action

Anticonvulsant. Mechanism of action is uncertain, but it may potentiate the action of GABA, an inhibitory neurotransmitter, or it may stabilize membranes and suppress propagation of seizures from an epileptic foci via changes in sodium and calcium conductance. Half-life in dogs has been reported to be approximately 15 hours in one study and 16 hours (plasma) to 57 hours (red blood cells [RBCs]) in another study. In cats, the half-life is longer than in dogs (33 hours).

## Indications and Clinical Uses

Zonisamide is used to treat refractory seizures in dogs when other drugs have not been effective. It has been effective in experimentally induced seizures in dogs and in approximately 50% of dogs with refractory epilepsy. It has been used as an add-on with other anticonvulsant drugs such as phenobarbital and potassium bromide.

## Precautionary Information

### Adverse Reactions and Side Effects

At the suggested clinical doses, adverse effects have not been reported for dogs, except for isolated case reports. Liver injury is possible and dogs should be monitored during treatment. Zonisamide is a sulfonamide drug, and dogs sensitive to sulfonamides may be at higher risk for reactions to zonisamide. Adverse reactions can include lethargy, ataxia, and vomiting. Like other anticonvulsants, ataxia, sedation, and CNS changes are possible. In safety studies, beagles received 75 mg/kg/day for 1 year with minimal side effects. In cats, adverse effects include mild gastrointestinal problems, sedation, and ataxia.

### Contraindications and Precautions

Because zonisamide resembles sulfonamides in structure, use cautiously in animals that are sensitive to these drugs. (See sulfonamide monographs in this book for full details on adverse effects.)

### Drug Interactions

When administered concurrently with phenobarbital, the half-life of elimination is more rapid for zonisamide, which may necessitate higher doses. It is expected to potentiate other central nervous system (CNS) depressants and anticonvulsants.

## Instructions for Use

Most experience with zonisamide in animals has been preliminary work in dogs with refractory epilepsy. Although low doses may produce plasma concentrations within the therapeutic range reported for people, when administered with phenobarbital,

drug concentrations may be lower because drug metabolism is increased. Zonisamide half-life was shorter in dogs receiving phenobarbital concurrently. These observations indicate that higher doses may be needed for combination therapy with phenobarbital compared with monotherapy. With chronic treatment some tolerance that reduces efficacy after 2-3 months may develop.

### **Patient Monitoring and Laboratory Tests**

Effective plasma concentrations in animals have been suggested to be 10-40 mcg/mL.

### **Formulations**

- Zonisamide is available in 25-, 50-, and 100-mg capsules.

### **Stability and Storage**

Store in a tightly sealed container, protected from light, and at room temperature. Stability of compounded formulations has not been evaluated.

### **Small Animal Dosage**

#### **Dogs**

- Start with 5 mg/kg q12h PO and increase gradually as needed to control seizures.
- 10 mg/kg q12h PO when added to phenobarbital treatment.

#### **Cats**

- Dose regimens have not been defined in cats, but 10 mg/kg has been used in experimental cats.

### **Large Animal Dosage**

- No dose has been reported for large animals.

### **Regulatory Information**

No regulatory information is available. For extralabel use withdrawal interval estimates, contact FARAD at 1-888-USFARAD (1-888-873-2723).

Racing Commissioners International (RCI) Classification: 3

## APPENDIX A

### Information for Pharmacists

#### Excipients in Medications or Human Drugs that May Be Harmful to Pets

Drug/Excipient/ Food	Species Affected	Toxicity	Reference
Acetaminophen	Dogs, cats	Hepatotoxicity (dogs) and red blood cell oxidative injury (cats)	Campbell A, Chapman M. <i>Handbook of Poisoning in Dogs and Cats</i> , Blackwell Science, Malden, MA, 2000, p. 31, 205.
Alcohols	Dogs, cats, birds	Central nervous system toxicity	Osweiler G, Carson T, Buck W, Van Gelder G. <i>Clinical and Diagnostic Veterinary Toxicology</i> 3rd ed. Kendall/Hunt, Dubuque, IA, 1976, p. 388.
Avocado	Birds	Pulmonary congestion; nonsuppurative in- flammation of the liver, kidney, pan- creas, skin, and proventriculus	LaBonde J. Avian toxicology. In Proceedings of the 2006 Association of Avian Veterinarians Meeting.
Benzocaine	Cats	Red blood cell oxidative injury, hemolytic anemia	Harvey J. Toxic hemolytic anemias. In Proceedings of the American College of Internal Medicine Meeting 2006.
Chamomile	Cats	Emesis, diarrhea, depression, lethargy, epistaxis	
Chocolate	Dogs, birds	Cardiovascular and central nervous system stimulation	Campbell A, Chapman M. <i>Handbook of Poisoning in Dogs and Cats</i> , Blackwell Science, Malden, MA, 2000, p 106.
Estrogen	Dogs	Bone marrow suppression	Campbell A, Chapman M. <i>Handbook of Poisoning in Dogs and Cats</i> , Blackwell Science, Malden, MA, 2000, p 245.
Ethyl glycols (diethylene glycol, ethyl- ene glycol)	Dogs, cats	Central nervous system toxicity, nephrotoxicity	Campbell A, Chapman M. <i>Handbook of Poisoning in Dogs and Cats</i> , Blackwell Science, Malden, MA, 2000, p 22, 127.
Fat, fatty foods	Dogs	Increased risk of pancreatitis	
Garlic/onions	Dogs, cats	Hemolytic anemia	Warman SM. Dietary intoxications. In Proceedings of the British Small Animal Veterinary Congress, 2007.

## Excipients in Medications or Human Drugs that May Be Harmful to Pets—cont'd

Drug/Excipient/ Food	Species Affected	Toxicity	Reference
Grapes/raisins	Dogs	Renal toxicity	Warman SM. Dietary intoxications. In Proceedings of the British Small Animal Veterinary Congress, 2007.
Macadamia nuts	Dogs	Neurotoxicity	Warman SM. Dietary intoxications. In Proceedings of the British Small Animal Veterinary Congress, 2007.
Macrolide antibiotics, oral route	Horses, rabbits	Diarrhea, enteritis, colic	Papich MG. Antimicrobial therapy for gastrointestinal diseases. <i>Veterinary Clinics of North America: Equine Practice</i> 2003 Dec;19(3):645–63 (Review).
Methylene blue	Cats	Red blood cell oxidative injury, hemolytic anemia	Harvey J. Toxic hemolytic anemias. In Proceedings of the American College of Internal Medicine Meeting 2006.
Nonsteroidal anti-inflammatory agents for humans (naproxen, ibuprofen)	Dogs, cats	Gastrointestinal ulceration and perforation, nephrotoxicity	Campbell A, Chapman M. <i>Handbook of Poisoning in Dogs and Cats</i> , Blackwell Science, Malden, MA, 2000, p 148, 192.
Pennyroyal	Cats	Hepatotoxicity	Wisner T. Toxicology of household products. In Proceedings of the International Veterinary Emergency and Critical Care Symposium, 2007.
Permethrin	Cats	Neuromuscular and central nervous system toxicity	Campbell A, Chapman M. <i>Handbook of Poisoning in Dogs and Cats</i> , Blackwell Science, Malden, MA, 2000, p 238.
Phenazopyridine	Cats	Hepatotoxicity and red blood cell oxidative injury	Harvey J. Toxic hemolytic anemias. In Proceedings of the American College of Internal Medicine Meeting 2006.
Phosphate enemas	Cats	Profound hypocalcemia	Wisner T. ASPCA Poison Control Center
Pseudoephedrine	Dogs, cats	Cardiovascular and central nervous system stimulation	Plumlee K. Poisons in the medicine cabinet. In Proceedings of the Western Veterinary Conference, 2004.
Raw yeast dough	Dogs	Alcohol poisoning, gastrointestinal dilatation and volvulus	Warman SM. Dietary intoxications. In Proceedings of the British Small Animal Veterinary Congress, 2007.

Continued

Excipients in Medications or Human Drugs that May Be Harmful to Pets—cont'd			
Drug/Excipient/ Food	Species Affected	Toxicity	Reference
Salt	Dogs, cats	Hypernatremia, central nervous system toxicity	Campbell A, Chapman M. <i>Handbook of Poisoning in Dogs and Cats</i> , Blackwell Science, Malden, MA, 2000, p. 42.
Tobacco prod- ucts	Dogs, cats	Muscle weakness, twitching, depression, tachycardia, shallow respiration, collapse, coma, cardiac arrest	Plumlee K. Household poisons. In Proceedings of the Western Veterinary Conference, 2004.
Xylitol	Dogs, birds	Profound hypoglycemia and hepatocellular necrosis	Wismer T. Hepatic toxins and the emergent patient. In Proceedings of the International Veterinary Emergency and Critical Care Symposium, 2006.

Acknowledgment: This table was created with the assistance of Gigi Davidson, RPh, North Carolina State University.

## APPENDIX B

### Prescription Writing Reference

#### Always Include

Prescribing veterinarian's name

Practice address

Practice telephone number

Drug Enforcement Administration (DEA) # (if written for a controlled substance)

Current date

Rx

- **Drug Name:** (Print FULL brand name or generic name—NEVER abbreviate)
- **Dosage Form:** (Specify tablet, capsule, suspension, other)
- **Strength:** (mg, g,  $\mu$ g, etc.) or concentration (mg/mL). Use metric units and use mcg for  $\mu$ g whenever possible.
- **Total Quantity:** (# 10 [for 10 tablets]; 60 mL)
- **Sig (Latin for “write on label”):** *Include the following:* Dose (individual), route, frequency, duration, indication, or use
- **Number of Refills:** Define the number legally permitted
- **Designate:** Whether or not generic substitution is permissible
- **Signature**

#### Owner Information

##### Always Include

- Patient's name (in “quotes”)
- Patient's age or date of birth
- Owner's name (or that of an owner representative)
- Owner's address
- Owner's phone number

#### Common Prescription Writing Errors to Avoid

- Always use metric units: for example, g (gram) for solids; ml or mL (milliliter) for liquids.
- Use per instead of a slash (/), which can be interpreted as the number 1.
- Write out “units” instead of the abbreviation u, which can be interpreted as 0 or 4 or micro.
- Use “once daily” instead of sid, which has been interpreted as 5/d or 5 per day. (NOTE: “sid” is not a conventional abbreviation recognized by pharmacists.)
- Use “three times daily” instead of tid, and use “four times daily” instead of qid.
- Use “every other day” instead of qod.
- AVOID CONFUSING ABBREVIATIONS—abbreviations like qd, qid, and qod are easily confused with each other

##### When writing numbers:

- Use a leading zero with decimals (e.g., use 0.5 mL rather than .5 mL).
- Avoid using a trailing zero (e.g., use 3 rather than 3.0).
- Spell out numbers in parentheses to avoid alterations.
- ALWAYS—When in doubt, spell it out.

## APPENDIX C

### Calculation of Drug Doses

How to Calculate Milliliters (mL) Needed

$$\text{Dose (mg/kg)} \times \text{kilograms body weight} = \text{total dose needed (mg)}$$

$$\text{Strength of solution (mg/mL)} = (\% \text{ strength}) \times 10$$

$$\frac{\text{Total dose needed}}{\text{Strength of solution (mg/mL)}} = \text{mL needed}$$

#### Example

20-kg dog needs 15 mg/kg of a 20% solution

$$20 \text{ kg} \times 15 \text{ mg/kg} = 300 \text{ mg total dose needed}$$

$$\text{Strength of solution} = 20\% \times 10 = 200 \text{ mg/mL}$$

$$\text{mL needed} = 300 \text{ mg} / 200 \text{ mg/mL} = 1.5 \text{ mL}$$

#### How to Calculate Tablets Needed

$$\text{Dose (mg/kg)} \times \text{kilograms body weight} = \text{total dose needed (mg)}$$

$$\frac{\text{Total dose needed}}{\text{Strength of tablet}} = \text{Number of tablets needed}$$

#### Example

20-kg dog needs 12 mg/kg

Tablet size is 100 mg

$$15 \text{ kg} \times 12 \text{ mg/kg} = 240 \text{ mg total dose needed}$$

$$240 \text{ mg} / 100 \text{ mg tablets} = 2.4 \text{ tablets}$$

(In most instances, you would round up to 2½ tablets if the medication has sufficient safety. \*Refer to the section on “splitting tablets” on page 863.)

#### How to Calculate Infusion Rates

$$\text{Dose (mg/kg/hour)} \times \text{kilograms body weight} = \text{total dose (mg) needed per hour}$$

If dose is listed in micrograms/kg/hour, multiply by 1000 for mg/kg/hour.

$$\text{Strength of solution (mg/mL)} = [\% \text{ strength}] \times 10$$

$$\text{mL Needed per Hour} = \frac{(\text{Total Dose Needed per Hour})}{(\text{Strength of Solution mg/mL})}$$

Administer the total mL to fluid administered in each hour interval. If fluid is to be administered over 24 hours: mL needed per hour  $\times$  24 = mL needed per day.

#### Example:

- 15-kg dog needs 2 mg/kg/hour of a 10% solution
- Fluid rate (lactated Ringer's solution) is 60 mL/kg/day
- $15 \text{ kg} \times 2 \text{ mg/kg/hour} = 30 \text{ mg needed per hour}$
- $\text{Strength of solution} = 10\% \times 10 = 100 \text{ mg/mL}$
- $\text{mL of drug needed per hour} = (30 \text{ mg per hour}) / (100 \text{ mg/mL}) = 0.3 \text{ mL per hour}$
- 0.3 mL of medication should be added to each hour of fluids to be administered
- Fluid rate is  $60 \text{ mL/kg/day} = 2.5 \text{ mL/kg/hr} = 37.5 \text{ mL/hr}$  for a 15-kg dog.

To each 37.5 mL/hr fluid volume to be infused, add 0.3 mL of medication. If drug is stable in solution for 24 hours, total amount can be added to a 24-hour volume of fluid:

- Total fluid needed per 24 hours =  $60 \text{ mL/kg/day} \times 15 \text{ kg} = 900 \text{ mL}$ .
- $0.3 \text{ mL per hour} \times 24 \text{ hours} = 7.2 \text{ mL per day}$  added to 900 mL total fluid requirement, or 8 mL added to each liter of fluids.

**When splitting tablets, when to round up and when to round down:**

Avoid trying to split a tablet into less than one fourth of a tablet. Smaller fractions cannot be accurately measured.

For “safe” drugs with high therapeutic index (e.g., antibiotics, nutritional supplements, hormones, antiparasitic agents, antacids), round up to the next highest tablet size or fraction of a tablet.

For drugs with narrow therapeutic index (cardiovascular drugs, nonsteroidal anti-inflammatory drugs, drugs that act on the central nervous system, anticancer agents, anticoagulants), round down to the next lowest tablet size or fraction of a tablet.



## **APPENDIX D**

### **Compounded Formulations: What to Look for to Detect Incompatibility or Instability**

#### **Liquid-Dose Forms**

Color change (amber to dark brown)  
Signs of microbial growth  
Cloudiness, haze, flocculent, or film formation  
Separation of phases (e.g., oil and water, emulsion)  
Precipitation, clumping, crystal formation  
Droplets or fog forming on inside of container  
Gas or odor release  
Swelling of container

#### **Solid-Dose Forms**

Odor (sulfur or vinegar odor)  
Excessive powder or crumbling  
Cracks or chips in tablets  
Swelling of tablets or capsules

#### **"Rules of Thumb"**

Do not mix drugs that require reconstitution in a vial with other drugs, and do not add other drugs to the vial.  
Do not mix drugs that are not in an aqueous vehicle (e.g., propylene glycol) with IV fluids.  
Do not mix hydrochloride (HCl) salts or drugs with buffers (citrates, bicarbonates, phosphates).  
Beyond-use-date for compounded drugs (the date after which a compounded preparation is not to be used) is 14 days for water-containing formulations (refrigerated), 6 months for nonaqueous liquids and solid formulations, and 60 days for other formulations. These times may be exceeded if there is valid scientific stability information.  
Whenever possible, compounded formulations should be prepared from a Food and Drug Administration–approved formulation.  
Compounded formulations should retain strength of  $\pm 10\%$  (that is, 90%-110%) of the nominal strength of the formulation.

## APPENDIX E

### Controlled Substance Charts: United States and Canada

Drug Examples	United States*
Heroin, LSD, peyote, marijuana, mescaline.	<p><i>Schedule I</i></p> <ul style="list-style-type: none"> <li>• High abuse potential</li> <li>• No currently accepted medical use</li> <li>• No veterinary uses identified</li> </ul>
Morphine and morphine derivatives and synthetic opioids. Drugs used in veterinary medicine include morphine, meperidine, etorphine, hydrocodone, hydromorphone, oxycodone, codeine (in some forms), hydrocodone, and pentobarbital.	<p><i>Schedule II</i></p> <ul style="list-style-type: none"> <li>• High abuse potential; potentially severe psychological or physical dependence</li> <li>• Currently accepted medical use but may be severely restricted</li> <li>• Telephone orders to a pharmacy are allowed only in emergencies if written prescription follows promptly</li> <li>• No refills allowed</li> </ul>
Drugs used in veterinary medicine include anabolic steroids (stanozolol, oxymetholone, testosterone, methyltestosterone, boldenone, trenbolone), barbiturates (thiamylal, thiopental), opioids (buprenorphine and codeine in some forms), and ketamine and derivatives (ketamine and tiletamine zolazepam).	<p><i>Schedule III</i></p> <ul style="list-style-type: none"> <li>• Abuse potential less than the drugs/substances in Schedules I and II; potentially moderate or low physical dependence or high psychological dependence</li> <li>• Currently accepted medical use</li> <li>• Telephone orders to pharmacy permitted</li> <li>• Veterinarian may authorize limited refills</li> </ul>
Drugs used in veterinary medicine include opioids (butorphanol and pentazocine), benzodiazepines (diazepam, oxazepam, midazolam, clonazepam, clorazepate, and alprazolam), and phenobarbital	<p><i>Schedule IV</i></p> <ul style="list-style-type: none"> <li>• Abuse potential relative to drugs/substances in Schedule III; potentially limited to physical or psychological dependence</li> <li>• Currently accepted medical use</li> <li>• Telephone orders to pharmacy permitted</li> <li>• Veterinarian may authorize limited refills</li> </ul>
Codeine preparations used as antitussives and some opioids used as antidiarrheals (e.g., diphenoxylate). Tramadol added in 2014.	<p><i>Schedule V</i></p> <ul style="list-style-type: none"> <li>• Lowest abuse potential; potentially very limited physical or psychological dependence</li> <li>• Currently accepted medical use</li> <li>• Veterinarian can determine refills</li> <li>• Some products containing limited amounts of Schedule V substances (e.g., cough suppressants) available over-the-counter</li> </ul>

\*Complete list for the United States can be located at [www.justice.gov/dea/pubs/scheduling.html](http://www.justice.gov/dea/pubs/scheduling.html).

Drug Examples	Canada
Sedatives such as barbiturates and derivatives (secobarbital), thiobarbiturates (pentothal sodium), and anabolic steroids	<i>Part G of the Food and Drug Regulation (FDR)</i> <ul style="list-style-type: none"> <li>Controlled drugs</li> <li>Misuse potential</li> <li>Verbal and written prescriptions under certain conditions</li> <li>Only prescribed if required for medical condition</li> <li>Specified number of refills (conditions apply)</li> <li>Records must be kept</li> <li>May be administered under emergency situations (conditions apply)</li> </ul>
Amphetamines	<i>Part G of the FDR</i> <ul style="list-style-type: none"> <li>Designated controlled drug</li> <li>May be used for designated medical conditions outlined in FDR</li> </ul>
Benzodiazepine tranquilizers, such as diazepam and lorazepam	<i>Benzodiazepines and Other Targeted Substances Regulations</i> <ul style="list-style-type: none"> <li>Misuse potential</li> <li>Verbal and written prescriptions under certain conditions</li> <li>Only prescribed if required for medical condition</li> <li>Specified number of refills (conditions apply)</li> <li>Records must be kept</li> <li>May be administered under emergency situations (conditions apply)</li> </ul>
Opiates: heroin, morphine, codeine (in some forms) and analgesics such as pentazocine and fentanyl	<i>Narcotic Control Regulation</i> <ul style="list-style-type: none"> <li>High misuse potential</li> <li>Written prescriptions for specific medical conditions†</li> <li>Records of opiate prescription file must be kept</li> <li>No refills (limited amounts in a prescription)</li> <li>Heroin and methadone are subject to specific controls</li> </ul>
LSD, mescaline (peyote), harmaline, psilocin, and psilocybin (magic mushrooms)	<i>Part J of the FDR</i> <ul style="list-style-type: none"> <li>Considered “restricted drugs”</li> <li>High misuse potential</li> <li>No recognized medical use</li> <li>Marijuana exemption from FDR if produced for medical reasons</li> </ul>

†Verbal prescriptions are permitted for certain opioid preparations (such as Tylenol No. 2 and No. 3) but not for opiate alone or opiates with one other active nonopioid ingredient.

## APPENDIX F

### Drugs for Infections Commonly Seen in Small Animals

Infection Site	First-Choice Drugs	Alternative-Choice Drugs
Skin: pyoderma or other skin infection	Amoxicillin + clavulanate Cephalosporin†, clindamycin	Trimethoprim + sulfonamides‡ Fluoroquinolone*, lincomycin, doxycycline or minocycline
Urinary tract	Cephalosporin† Amoxicillin + ampicillin Amoxicillin + clavulanate	Trimethoprim + sulfonamides‡ Fluoroquinolone* Tetracycline
Respiratory tract	Amoxicillin + clavulanate Fluoroquinolone* Cephalosporin†	Macrolide (azithromycin) Aminoglycosides (amikacin, gentamicin) Doxycycline or minocycline Clindamycin Trimethoprim + sulfonamides‡ Chloramphenicol Extended-spectrum cephalosporin§
Septicemia¶	Amoxicillin + clavulanate Cephalosporin† Fluoroquinolone Aminoglycoside	Extended-spectrum cephalosporin§ Piperacillin + tazobactam Carbapenem
Bone and joint	Cephalosporin† Amoxicillin + clavulanate	Trimethoprim + sulfonamides‡ Clindamycin Extended-spectrum cephalosporin§ Fluoroquinolone*
Intracellular pathogens	Doxycycline or minocycline Fluoroquinolone*	Azithromycin Clindamycin

\*Fluoroquinolone includes enrofloxacin, marbofloxacin, orbifloxacin, or pradofloxacin (pradofloxacin not approved for dogs in US).

†Cephalosporin includes cephalixin, cefpodoxime proxetil, cefadroxil or cefovecin.

‡Trimethoprim in combination with sulfonamides includes trimethoprim in combination with sulfadiazine, trimethoprim in combination with sulfamethoxazole, or ormetoprim in combination with sulfadimethoxine.

§Extended-spectrum cephalosporin can include either second-generation or third-generation drugs (e.g., ceftazidime, ceftiofur, cefotaxime).

¶Combinations of drugs are often used in acute febrile septicemia. Such combinations may include a beta-lactam plus an aminoglycoside or a fluoroquinolone plus amoxicillin + clavulanate.

## APPENDIX G

## Antibiotic Drug Selection for Equine Bacterial Pathogens

Pathogen	Drug Choice	Alternative Choice
<b>Gram-Positive</b>		
<i>Rhodococcus equi</i>	Erythromycin ± rifampin, azithromycin	Clarithromycin
<i>Streptococcus</i> spp.	Penicillin G, ampicillin, ceftiofur, trimethoprim-sulfadiazine	Erythromycin, chloramphenicol
<i>Staphylococcus aureus</i>	Trimethoprim + sulfonamide	Enrofloxacin, orbifloxacin, chloramphenicol, gentamicin
<b>Gram-Negative</b>		
<i>Escherichia coli</i>	Gentamicin, amikacin	Ceftiofur, enrofloxacin, orbifloxacin, marbofloxacin, trimethoprim + sulfonamide
<i>Klebsiella pneumoniae</i>	Gentamicin, amikacin	Ceftiofur, enrofloxacin, orbifloxacin, marbofloxacin, trimethoprim + sulfonamide
<i>Enterobacter</i> spp.	Gentamicin, amikacin	Ceftiofur, enrofloxacin, trimethoprim + sulfonamide
<i>Pseudomonas aeruginosa</i>	Gentamicin, amikacin, piperacillin + tazobactam	Enrofloxacin, marbofloxacin, cefepime, ceftazidime
<i>Pasteurella</i> spp.	Ampicillin, ceftiofur, trimethoprim + sulfonamide	Enrofloxacin, orbifloxacin, marbofloxacin, chloramphenicol, tetracycline
<i>Actinobacillus</i> spp.	Ampicillin, penicillin, trimethoprim + sulfonamides	Enrofloxacin, amikacin, gentamicin, ceftiofur
<b>Anaerobes</b>		
<i>Clostridium</i> , <i>Fusobacterium</i> , <i>Peptostreptococcus</i> , <i>Bacteroides</i> spp.	Metronidazole, penicillin G	Chloramphenicol, or cefoxitin (injectable)
<b>Other</b>		
<i>Lawsonia intracellularis</i>	Oxytetracycline, doxycycline (doxycycline, oral only)	Chloramphenicol, erythromycin, clarithromycin, azithromycin
<i>Ehrlichia</i>	Oxytetracycline, doxycycline (doxycycline, oral only)	Chloramphenicol
<i>Neorickettsia risticii</i> (Potomac horse fever)	Oxytetracycline, doxycycline (doxycycline, oral only)	

## APPENDIX H

### Drugs That May Induce Cytochrome P450 Enzymes

- Alcohol
- Chlorinated hydrocarbons
- Diazepam (Valium)
- Diphenhydramine
- Estrogens
- Griseofulvin
- Hyperthyroidism
- Pentobarbital
- Phenobarbital
- Phenylbutazone
- Phenytoin (Dilantin)
- Progestogens
- Rifampin
- St. John's wort

## **APPENDIX I**

### **Drugs That May Inhibit Cytochrome P450 Enzymes**

- Amiodarone
- Chloramphenicol
- Cimetidine
- Cisapride
- Clarithromycin
- Cyclophosphamide
- Diltiazem
- Erythromycin
- Felbamate
- Fluoroquinolones
- Interferon (vaccines)
- Itraconazole
- Ketoconazole
- Omeprazole
- Organophosphates
- Phenylbutazone
- Quinidine
- Tetracycline
- Verapamil
- Voriconazole

## APPENDIX J

### Drugs That May Inhibit the P-Glycoprotein Membrane Transporter Coded by ABCB1 (formerly known as MDR1)

- Bromocriptine
- Carvedilol
- Chlorpromazine
- Cyclosporine
- Diltiazem
- Erythromycin
- Fluoxetine
- Grapefruit juice
- Itraconazole
- Ketoconazole
- Methadone
- Paroxetine
- Pentazocine
- Quinidine
- Spinosad
- St. John's wort
- Tamoxifen
- Verapamil

#### References

- Mealey KL, 2013 Mealey KL Adverse drug reactions in veterinary patients associated with drug transporters *Veterinary Clinics of North America: Small Animal Practice* 43:2013:1067-1078
- Mealey KL & Fidel J, 2015 Mealey KL & Fidel JP-glycoprotein mediated drug interactions in animals and humans with cancer *Journal of Veterinary Internal Medicine* 29:2015:16



**APPENDIX K****Drugs That Are Substrates for the P-Glycoprotein Membrane Transporter Coded by ABCB1 (formerly known as MDR1)**

- Acepromazine
- Aldosterone
- Amitriptyline
- Butorphanol
- Cortisol
- Cyclosporine
- Dexamethasone
- Digoxin
- Diltiazem
- Doramectin
- Doxorubicin
- Doxycycline
- Erythromycin
- Itraconazole
- Ivermectin
- Ketoconazole
- Levofloxacin
- Loperamide
- Methylprednisolone
- Milbemycin
- Morphine
- Moxidectin
- Ondansetron
- Phenothiazines
- Selamectin
- Tacrolimus
- Terfenadine
- Tetracycline
- Verapamil
- Vinblastine
- Vincristine

**References**

- Mealey KL, 2013 Mealey KL Adverse drug reactions in veterinary patients associated with drug transporters *Veterinary Clinics of North America: Small Animal Practice* 43:2013:1067-1078
- Mealey KL & Fidel J, 2015 Mealey KL & Fidel JP-glycoprotein mediated drug interactions in animals and humans with cancer *Journal of Veterinary Internal Medicine* 29:2015:16

## APPENDIX L

### Fluid Solution Composition

Solution Type	Na <sup>+</sup> (mEq/L)	K <sup>+</sup> (mEq/L)	Cl <sup>-</sup> (mEq/L)	Ca <sup>++</sup> (mEq/L)	Mg <sup>++</sup> (mEq/L)	Buffer (mEq/L)	Osmolarity (mOsm/L)	pH
Ringer's solution	147	4	156	4	0	0	310	5-7.5
Lactated Ringer's solution	131	5.4	111	2	0	29 (lactate)	280.6	6-7.5
0.9 % NaCl	154	0	154	0	0	0	308	4-5
5% dextrose	0	0	0	0	0	0	252	4-6.5
2.5% dextrose /0.45% NaCl	77	0	77	0	0	0	280	4-5
Plasma-Lyte	140	5	98	0	3	27 (acetate)	294	4-6.5
Dextran 6% and 0.9% NaCl	154	0	154	0	0	23 (gluconate)	310	3.0-7.0
Hetastarch	154	0	154	0	0	0	309	5.5
Pentastarch	154	0	154	0	0	0	326	5.0
Hemoglobin glutamer (oxyglobin)							300	7.8
Normosol-R	140	5	98	0	3	27 (acetate) 23 (gluconate)	294	6.6

## APPENDIX M

## How to Report an Adverse Drug Reaction

1. Phone the drug sponsor to report an adverse drug experience (ADE) if it is a Food and Drug Administration (FDA)–approved animal drug. Obtain drug sponsor phone numbers from the product label or from the company’s website. When phoning the pharmaceutical company, inform them that you wish to speak with a veterinarian on their staff to report an ADE.

Contact the FDA and complete Form 1932a. This form may be completed regardless of whether the drug is an animal-approved drug or human-approved drug. The FDA can be contacted from their website at: <http://www.fda.gov/Animal>

[Veterinary/SafetyHealth/ReportProblem/ucm055305.htm](http://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportProblem/ucm055305.htm)

The FDA also may be contacted at this address:

Document Control Unit (HFV-199)

Attention: Division of Veterinary Product Safety

Center for Veterinary Medicine

Food and Drug Administration

7500 Standish Place

Rockville, MD 20855-2764

Telephone: 1-888-FDA-VETS (888-332-8387)

When completing Form 1932a, supply as much history and clinical data as possible, including concurrent medications administered to the animal.

## 2. **Animal Biologics: Vaccines, Bacterins:**

Contact the U.S. Department of Agriculture (USDA) Center for Veterinary Biologics (CVB):

Telephone (800) 752-6255, or visit their website at:

<http://www.aphis.usda.gov/wps/portal/aphis/home/>

From the website, obtain the AER worksheet, which may be faxed or mailed to the CVB at this address:

Center for Veterinary Biologics

1920 Dayton Avenue

P.O. Box 844

Ames, Iowa 50010

Fax: (515) 337-6120

## 3. **Pesticides: Topically Applied External Parasiticides**

Contact the U.S. Environmental Protection Agency (EPA):

Office of Pesticide Programs, Mail Code 7506C

1200 Pennsylvania Ave. NW

Washington, DC 20460

(800) 858-PEST (800-858-7378)

[www.epa.gov/pesticides/](http://www.epa.gov/pesticides/)

or

<http://www2.epa.gov/pets/forms/contact-us-about-pets>

## APPENDIX N

### Drugs Prohibited from Use in Food-Producing Animals

Because they present a risk to public health, the following drugs are prohibited in food-producing animals:

- Chloramphenicol
- Clenbuterol
- Diethylstilbestrol (DES)
- Dimetridazole
- Furazolidone
- Nitrofurazone (and other nitrofurans)
- Fluoroquinolones (extralabel use)
- Cephalosporins (not including cephalirin in cattle, swine, chickens, or turkeys):  
(1) For disease prevention purposes; (2) At unapproved doses, durations, or routes of administration; or (3) If the drug is not approved for that species and production class.
- Glycopeptide antibiotics (e.g., vancomycin)
- Iprnidazole (and other nitroimidazoles)
- Phenylbutazone in female dairy cattle less than 20 months of age
- Sulfonamide drugs in lactating dairy cattle\*
- Adamantane and neuraminidase inhibitor classes of drugs approved for treating or preventing influenza A are prohibited therapy in chickens, turkeys, and ducks.

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\*With the exception of sulfadimethoxine, sulfabromomethazine, and sulfaethoxyypyradazine, approved for use in some feeds.

## APPENDIX O

### Performance Horse Drug Regulations and Restrictions Association of Racing Commissioners International, Inc., Uniform Classification Guidelines for Foreign Substances (Revised April 2015)

The following definitions, regulations, and restrictions are adapted from the Racing Commissioners International website: [www.arci.com](http://www.arci.com) and the FEI Clean Sport Prohibited Substances List: <http://www.feicleansport.org/>

The RCI Drug Classification Scheme is based on (1) pharmacology, (2) drug use patterns, and (3) the appropriateness of a drug for use in the racing horse.

#### Classification Definitions

##### Class 1

Stimulant and depressant drugs that have the highest potential to affect performance and that have no generally accepted medical use in the racing horse. Many of these agents are Drug Enforcement Administration (DEA) Schedule II substances. These include the following drugs and their metabolites: opiates, opium derivatives, synthetic opioids and psychoactive drugs, amphetamines, and amphetaminelike drugs, as well as related drugs, including but not limited to, apomorphine, nikethamide, mazindol, pemoline, and pentylenetetrazol. Though not used as therapeutic agents, all DEA Schedule I agents are included in Class 1 because they are potent stimulant or depressant substances with psychotropic and often habituating actions.

##### Class 2

Drugs that have a high potential to affect performance but less of a potential than drugs in Class 1. These drugs are (1) not generally accepted as therapeutic agents in racing horses; or (2) they are therapeutic agents that have a high potential for abuse. Drugs in this class include psychotropic drugs, certain nervous system and cardiovascular system stimulants, depressants, and neuromuscular blocking agents. Injectable local anesthetics are included in this class because of their high potential for abuse as nerve blocking agents.

##### Class 3

Drugs that may or may not have generally accepted medical use in the racing horse, but the pharmacology of which suggests less potential to affect performance than drugs in Class 2. Drugs in this class include bronchodilators, anabolic steroids and other drugs with primary effects on the autonomic nervous system, procaine, antihistamines with sedative properties, and the high-ceiling diuretics.

##### Class 4

This class includes therapeutic medications that would be expected to have less potential to affect performance than those in Class 3. Drugs in this class include less potent diuretics, corticosteroids, antihistamines and skeletal muscle relaxants without prominent central nervous system (CNS) effects, expectorants and mucolytics, hemostatics, cardiac glycosides and antiarrhythmics, topical anesthetics, antidiarrheals, and mild analgesics. This class also includes the nonsteroidal anti-inflammatory drugs (NSAIDs) at concentrations greater than established limits.

**Class 5**

This class includes those therapeutic medications for which concentration limits have been established by the racing jurisdictions, as well as certain miscellaneous agents, and other medications as determined by the regulatory bodies. Included specifically are agents that have very localized actions only, such as antiulcer drugs and certain antiallergic drugs. The anticoagulant drugs are also included.

**Prohibited Substances in Racing Horses**

- A) The possession and/or use of a drug, substance, or medication, specified here, on the premises of a facility under the jurisdiction of the regulatory body for which a recognized analytical method has not been developed to detect and confirm the administration of such substance; or the use of which may endanger the health and welfare of the horse or endanger the safety of the rider or driver; or the use of which may adversely affect the integrity of racing:
  - 1) Erythropoietin
  - 2) Darbepoetin
  - 3) Oxyglobin
  - 4) Hemopure
- B) The possession and/or use of a drug, substance, or medication on the premises of a facility under the jurisdiction of the regulatory body that has not been approved by the U.S. Food and Drug Administration (FDA) for use in the United States.
- C) The practice, administration, or application of a treatment, procedure, therapy, or method identified here, which is performed on the premises of a facility under jurisdiction of a regulatory body and which may endanger the health and welfare of the horse or endanger the safety of the rider or driver; or the use of which may adversely affect the integrity of racing.

**Equine Prohibited Drugs: FEI Clean Sport Prohibited Substances Database (Revised April 2015).**

FEI (Fédération Equestre Internationale) has published guidelines to assist veterinarians to make a distinction between the use of routine, legitimate medication and deliberate and calculated doping to affect a horse's performance. The prohibited substance searchable database is available at:

<http://prohibitedsubstancesdatabase.feicleansport.org/>

Or access the FEI Clean Sport Prohibited Substances List (updated January 2015) at this website: <http://www.fei.org/fei/cleansport>

## APPENDIX P

### Important Internet Sites for Drug Information

**Drug Compounding: FDA Guidance #230 (2015 revision)**

<http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM446862.pdf>

**Drug Interactions**

<http://www.fda.gov/drugs/developmentapprovalprocess/developmentresources/ucm080499.htm>

**FDA Home Page**

<http://www.fda.gov/AnimalVeterinary/default.htm>

**FDA Adverse Drug Reports: Cumulative Summary**

<http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm055369.htm>

**FDA Adverse Drug Reaction Reporting Site**

<http://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm055305.htm>

**FDA-Approved Animal Drug Products: Animal Drugs @ FDA**

[www.accessdata.fda.gov/scripts/animaldrugsatfda/](http://www.accessdata.fda.gov/scripts/animaldrugsatfda/)

**FDA-Approved Human Drug Products: Drugs @ FDA**

[http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Search\\_Drug\\_Name](http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Search_Drug_Name)

**AAVPT USP Veterinary Drug Information**

<http://www.aavpt.org/>

**Extralabel (Off-label) Drug Use Information**

<https://www.avma.org/KB/Resources/Reference/Pages/AMDUCA.aspx>

**U.S. Drug Enforcement Administration (DEA) Controlled Substances Drug Schedules**

<http://www.deadiversion.usdoj.gov/schedules/index.html>

**Euthanasia Formulations and References (Updated 2013)**

<https://www.avma.org/KB/Policies/Pages/Euthanasia-Guidelines.aspx>

## APPENDIX Q

### Solution Compatibility Chart

Intravenous Medication	D2 1/2W	D5W	D10W	D5/1/4NS	D5/1/2NS	D5NS	NS	1/2NS	R	LR	D5R	D5LR	Dextran 6%/D5W/NS	Fruc 10%/W/NS	Invert sug 10%/W/NS	Na lactate 1/6 M
Acetazolamide	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Acyclovir		C		C	C	C	C				C					
Aminophylline	C	C	C	C	C	C	C	C	C	C	C	C	C	C		
Ammonium chloride							C									
Amikacin		C					C									
Amphotericin B		C														
Ampicillin		C					C									
Ascorbic acid	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Calcium chloride		C	C	C	C	C	C		C	C	C					
Calcium gluconate		C	C			C	C			C	C	C		W		C
Cefazolin Na		C	C	C	C	C	C	C	C	C	C				W	
Cefotaxime Na		C	C	C	C	C	C			C					W	C
Cefotetan		C					C									
Cefoxitin Na		C	C	C	C	C	C		C	C	C					C
Ceftazidime		C	C	C	C	C	C		C	C					W	C

Continued







Intravenous Medication	D2 1/2W	D5W	D10W	D5/1/4NS	D5/1/2NS	D5NS	NS	1/2NS	R	LR	D5R	D5LR	Dextran 6%/D5W/NS	Fruc 10%/W/NS	Invert sug 10%/W/NS	Na lactate 1/6 M
Potassium chloride	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Potassium phosphate	C	C	C	C	C	C	C	C					C	C	C	C
Prochlorperazine	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Propranolol	C <sup>p</sup>				C	C	C	C		C						
Ranitidine	C	C	C		C	C	C			C						
Sodium bicarbonate	C	C	C	C	C	C	C	C			C	C	C	C	C	
Sodium chloride	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Thiamine	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Thiopental	C	C	C	C	C	C <sup>6</sup>	C	C					C			C
Ticarcillin		C					C			C						
Tobramycin	C	C					C									
Warfarin			C		C	C	C				C					
Zidovudine	C <sup>p</sup>						C									

C, compatible; W, Compatible in water only; NS, compatible in normal saline only; C with a superscript number indicates the number of hours for which a solution is compatible and stable; C<sup>p</sup> indicates the preferred diluent; no entry, no documented information.

Abbreviations: D 2 1/2W: 2.5% dextrose in water; D5W: 5% dextrose in water; D10W: 10% dextrose in water; D5 1/4 NS: 5% dextrose and one-quarter strength (25%) normal saline; D5 1/2 NS: 5% dextrose in one-half normal saline; D5NS: 5% dextrose in normal saline; NS: normal saline (0.9% NaCl); 1/2 NS: one-half (50%) normal saline; R: Ringer's solution; LR: lactated Ringer's solution; D5R: 5% dextrose in Ringer's solution; D5LR: 5% dextrose in lactated Ringer's solution; Dextran 6%/D5W/NS: 6% Dextran in 5% dextrose in water and normal saline; Fruc 10%/W/NS: 10% fructose in water and normal saline; Invert sug 10%/W/NS: 10% inverted sugar in water and normal saline; Na lactate 1/6 M: sodium lactate one-sixth molar.

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## Conversion Information

### Weights and Measures

#### Prefixes for Fractions

deci =  $10^{-1}$

centi =  $10^{-2}$

milli =  $10^{-3}$

micro =  $10^{-6}$

nano =  $10^{-9}$

pico =  $10^{-12}$

#### Temperature Measures

$8^{\circ}\text{C} = 5/9 \times (8^{\circ}\text{F} - 32)$

$8^{\circ}\text{F} = 9/5 \times (8^{\circ}\text{C}) + 32$

#### Percentage Equivalents

0.1% solution contains 1 mg per mL

1% solution contains 10 mg per mL

10% solution contains 100 mg per mL

#### Milliequivalent Conversions

1 mEq Na = 23 mg Na = 58.5 mg NaCl

1 g Na = 2.54 g NaCl = 43 mEq Na

1 g NaCl = 0.39 g Na = 17 mEq Na

1 mEq K = 39 mg K = 74.5 mg KCl

1 g K = 1.91 g KCl = 26 mEq K

1 g KCl = 0.52 g K = 13 mEq K

1 mEq Ca = 20 mg Ca

1 g Ca = 50 mEq Ca

1 mEq Mg = 0.12 g  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$

1 g Mg = 10.2 g  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$  = 82 mEq Mg

10 mmol  $\text{P}_i$  = 0.31 g  $\text{P}_i$  = 0.95 g  $\text{PO}_4$

1 g  $\text{P}_i$  = 3.06 g  $\text{PO}_4$  = 32 mmol  $\text{P}_i$

### Metric Conversions

#### Volume Measurements

Teaspoonful = 5 mL

Tablespoonful = 15 mL

Fluid ounce = 30 mL

Pint = 473 mL

Quart = 946 mL

#### Linear Measurements

1 mm = 0.04 in

1 in = 25.4 mm = 2.54 cm

1 m = 39.4 in

1 in = 0.025 m

### Weight Measurements

1 mg = 0.017 grain

1 grain = 65 mg

1 g = 0.035 oz

1 oz = 28.3 g

1 kg = 2.2 lb

1 lb = 0.45 kg

### Weights and Equivalents: Metric System

#### Weight

kilogram = kg = 1000 grams

gram = g = 1 gram

milligram = mg = 0.001 gram

microgram = mcg = 0.001 milligram

#### Volume

liter = L = 1 L

milliliter = mL = 0.001 L

#### Avoirdupois Weight

1 ounce (oz) = 437.5 grains

1 pound (lb) = 16 ounces = 7000 grains

### Metric and Apothecary Equivalents

#### Exact Weight Equivalents

Metric	Apothecary
1 mg	1/64.8 grain
64.8 mg	1 grain
324 mg	5 grains
1 g	15.432 grains
31.103 g	1 ounce (480 grains)

#### Exact Volume Equivalents

Metric	Apothecary
1.00 mL	16.23 minims
3.69 mL	1 fluidram (60 minims)
29.57 mL	1 fluid ounce (480 minims)
473.16 mL	1 pint (7680 minims)
946.33 mL	1 quart (15,360 minims)



## Conversion of Body Weight

### Kilograms to Pounds and to Body Surface Area in Square Meters

Body Weight in Kilograms	Body Weight in Pounds	Body Surface Area in Square Meters	Body Weight in Kilograms	Body Weight in Pounds	Body Surface Area in Square Meters
1	2.2	0.1	36	79.37	1.11
2	4.41	0.16	37	81.57	1.13
3	6.61	0.21	38	83.77	1.15
4	8.82	0.26	39	85.98	1.17
5	11.02	0.3	40	88.18	1.19
6	13.23	0.33	41	90.39	1.21
7	15.43	0.37	42	92.59	1.22
8	17.64	0.41	43	94.8	1.24
9	19.84	0.44	44	97	1.26
10	22.05	0.47	45	99.21	1.28
11	24.25	0.5	46	101.41	1.3
12	26.46	0.53	47	103.62	1.32
13	28.66	0.56	48	105.82	1.34
14	30.86	0.59	49	108.03	1.36
15	33.07	0.62	50	110.23	1.38
16	35.27	0.64	51	112.43	1.39
17	37.48	0.67	52	114.64	1.41
18	39.68	0.7	53	116.84	1.43
19	41.89	0.72	54	119.05	1.45
20	44.09	0.75	55	121.25	1.47
21	46.3	0.77	56	123.46	1.48
22	48.5	0.8	57	125.66	1.5
23	50.71	0.82	58	127.87	1.52
24	52.91	0.84	59	130.07	1.54
25	55.12	0.87	60	132.28	1.55
26	57.32	0.89	61	134.48	1.57
27	59.52	0.91	62	136.69	1.59
28	61.73	0.93	63	138.89	1.61
29	63.93	0.96	64	141.09	1.62
30	66.14	0.98	65	143.3	1.64
31	68.34	1	66	145.5	1.66
32	70.55	1.02	67	147.71	1.67
33	72.75	1.04	68	149.91	1.69
34	74.96	1.06	69	152.12	1.71
35	77.16	1.08	70	154.32	1.72

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## Important Contact Information for Veterinary Drugs

### Animal Blood Banks

Animal Blood Resources International: Animal Blood Bank Hotline: 800-243-5759; a 24-hour hotline that focuses on transfusion medicine (particularly blood component therapy), recommending dosages and infusion rates.

Veterinarian's Blood Bank: (877) 838-8533

Pet Blood Bank: Critical Care Specialist: (970) 347-1017

HEMOPET: (714) 891-2022

A national, full-service, nonprofit blood bank and educational network for animals; accessible 24 hours.

### Poison Control Centers

ASPCA National Animal Poison Control Center: 888-4ANI-HELP (888-426-4435). Fee charged for each case.

PET POISON HELPLINE: (800) 213-6680

A 24-hour nationwide service offered by the Pet Poison Center. Available to pet owners and veterinary professionals. A fee per case is charged.

VET P.E.T.S (Veterinary Poison Emergency Treatment Services): (800)572-5842.

A 24-hour nationwide service. Fee charged for each case.

### Drug Enforcement Agency (DEA)

Office of Diversion Control, Registration Section: 800-882-9539

### Food and Drug Administration Center for Veterinary Medicine (FDA/CVM): (240) 276-9300

**Food Animal Residue Avoidance Databank (FARAD):** 888-USFARAD (888-873-2723); Web site: [www.farad.org](http://www.farad.org). To send comments or question to FARAD, please do so by sending an e-mail to [USFarad@gmail.com](mailto:USFarad@gmail.com). Please do not send any extra-label drug use questions to this e-mail address. FARAD is sponsored by the USDA to prevent residues of drugs and other chemicals in food animals.

# Syringe Compatibility Table

	Atropine	Buprenorphine	Butorphanol	Chlorpromazine	Cimetidine	Codeine	Diazepam	Dimenhydrinate	Diphenhydramine	Fentanyl	Glycopyrrolate	Haloperidol lactate	Heparin	Hydroxyzine	Meperidine	Metoclopramide	Midazolam	Morphine	Pentazocine	Pentobarbital	Prochlorperazine	Promethazine	Ranitidine
Atropine	*			C	C				C	C	C		C	C	C	C	C	C	C	C	C	C	C
Buprenorphine		*																					
Butorphanol			*	C	C			I	C	C				C	C	C	C	C	C	C	C	C	I
Chlorpromazine				*	I			I	C	C	C		I	C	C	C	C	C	C	C	C	C	
Cimetidine					*		C		C	C	C		C	C	C		C	C	C	C	C	C	
Codeine						*				C	C			C	C		C	C	C	C	C	C	
Diazepam							*						I										I
Dimenhydrinate								*	C	C	I		I	C	C	C	I	C	C	C	I	C	C
Diphenhydramine									*	C	C	I		C	C	C	C	C	C	C	C	C	C
Fentanyl										*				C	C	C	C	C	C	C	C	C	C
Glycopyrrolate											*			C	C	C	C	C	C	C	C	C	C
Haloperidol lactate												*	I	I		C		I	C	C	C	C	C
Heparin										C		I	*		I	C		C	C	C	C	C	I
Hydroxyzine										C	C	I		*	C	C	C	C	C	C	C	C	I
Meperidine										C	C	I		C	*	C	C	C	C	C	C	C	C
Metoclopramide										C	C			C	C	*	C	C	C	C	C	C	C
Midazolam										C	C			C	C	C	*	C	C	C	C	C	C
Morphine		C								C	C	I		C	C	C	C	*	C	C	C	C	C
Pentazocine										C	C			C	C	C	C	C	C	C	C	C	C
Pentobarbital										I	I			I	I	C	I	I	C	*	I	I	I
Prochlorperazine										C	C			C	C	C	I	C	C	C	C	C	C
Promethazine										C	C			C	C	C	C	C	C	C	C	*	C
Ranitidine							I			C	C	C		I	C	C	I	C	C	C	C	C	*

Based on information in Trissel LA: Handbook on injectable drugs, ed 11, American Society of Health-System Pharmacists, Inc. The syringe compatibility table provides physical compatibility information on ly for drugs mixed in a syringe. Therapeutic incompatibilities are not represented, therefore, professional judgment should be exercised when utilizing this table. C, compatible; I, incompatible; no entry, no documented information.